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BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 5 1953

BRONCHIAL CARCINOMA: INCIDENCE AND AETIOLOGY*

BY

RICHARD DOLL, M.D., M.R.C.P.

Member of the Statistical Research Unit of the Medical Research Council

A little over a hundred years ago Dr. Gavin Milroy took an active part in the establishment of the Epidemiological Society. The object of the Society was to study "epidemic and endemic diseases, with special reference to the investigation of (*a*) the various external or physical agencies, and the different conditions of life, which favour their development or influence their character, and (*b*) the sanitary and hygienic measures best fitted to check, mitigate, or prevent them." In 1850, interest was focused on the great epidemic diseases, but the methods Milroy urged—the collection of statistical data on the natural history of disease over large areas and over periods of years followed by inductive reasoning from the observed facts—are as applicable to-day to the study of lung cancer as they were then to the study of plague, typhus, and cholera. And the rapid increase which has been recorded in the mortality from lung cancer suggests that it is urgent to determine the measures "best fitted to check, mitigate, or prevent" it.

Incidence

No figures are available for assessing the incidence of lung cancer in Britain, other than the mortality statistics of the Registrars-General. Because of its great fatality, the number of persons dying from it is nearly equal to the number affected, and, from this point of view, mortality statistics provide a reasonable estimate of the incidence. They are, however, subject to the inaccuracy inherent in the certification of causes of death.

The salient feature of the reported mortality is the extent to which it has increased in the last 50 years—and particularly in the last 25 years. In 1900 the crude annual death rate attributed to lung cancer in England and Wales was 8 per million persons; by 1925 it had risen to 20 and by 1950 to 278 per million.† In other words, the recorded rate increased two and a half times in the first 25 years, and 14 times in the next 25 years.

By 1950, 12,241 deaths were attributed to lung cancer in one year—10,254 in men and 1,987 in women. As a site of cancer, in both sexes taken together, the lung was second in importance to the stomach, but it was easily the most important site in men—giving rise to 28% more deaths than were attributed to cancer of the stomach and to more than double the number attributed to cancer of the colon. Of all cancers in men, 24% were classified as having arisen in the lung, but at ages 45–54, when lung cancer was relatively most frequent in proportion to other cancers, the proportion was 40%.

Compared with non-malignant diseases, lung cancer was recorded as a more common cause of death in men than hypertension or respiratory tubercle; but only a third as many deaths were attributed to it as were attributed to coronary artery disease. Of all male deaths in 1950, 4% were attributed to lung cancer; at ages 45–54 the proportion was 10%.

There is no reason to suppose that these figures have yet reached their maxima. On the contrary, the trend in mortality rates suggests that lung cancer will reach an even more prominent position. It is difficult to estimate the actual number of deaths which will occur. Trends do not always continue smoothly. For example, the trend in male mortality at ages 35–44 showed an almost steady increase from 1920 to 1946, when the rate reached the level of 166 deaths per million men. In 1950 the rate might have been expected to be about 190 per million, whereas in fact it remained the same as four years earlier. If future experience proves that the mortality in men aged 35–44 has, in fact, become stable, it is to be expected that the increase will also cease in the older age groups, but only after progressively longer periods of time have elapsed.

The maximum mortality from lung cancer, unlike that from every other major form of cancer in men, is not in the oldest age group. At present it lies in the age group 65–74, and in 1931–47 was a decade earlier (Fig. 1). Over the last 20 years the age distribution has become somewhat closer to that of the other major forms of cancer. If it can be assumed that the death rates under the age of 45 have now become stable, and that the trend in the age distribution continues until the distribution is similar to that of, say, cancer of the stomach, a rough estimate can be made of the number of deaths which will eventually be attributed to lung cancer. On such assumptions—admittedly highly speculative but, I think, not wholly unreasonable—the number of deaths, for a population of the same age and sex composition as at present, will eventually reach 20,000. In fact, the future population will almost certainly contain a higher proportion of old persons, so that the number recorded in 20 years' time may be as great as 25,000.

Increase in Incidence

The evidence that lung cancer has become more frequent derives from necropsy studies as well as from vital statistics and clinical series. Figures from Leeds General Infirmary

*The Milroy Lectures delivered at the Royal College of Physicians of London on February 10 and 12, 1953. (*Abridged.*)

†By 1952, the rate had reached the level of 321 per million.

published by Bonser (1934) and brought up to date by Watkinson (personal communication) show a rise in the proportion of necropsies at which a bronchial carcinoma was found from 1.4% in 1928–32 to 4.0% in 1949, and from 7.5% of all cancers found at necropsy to 16.9%. Figures from St. Mary's, St. Bartholomew's, and the Glasgow Western Infirmary also show increases over the last 15 years (Daff, Doll, and Kennaway, 1951). The only contrary experience recently recorded is that of Bryson and Spencer (1951); earlier reports are purposely not considered, as they would not seem to be relevant to a problem which has presented itself in an acute form only since they were written.

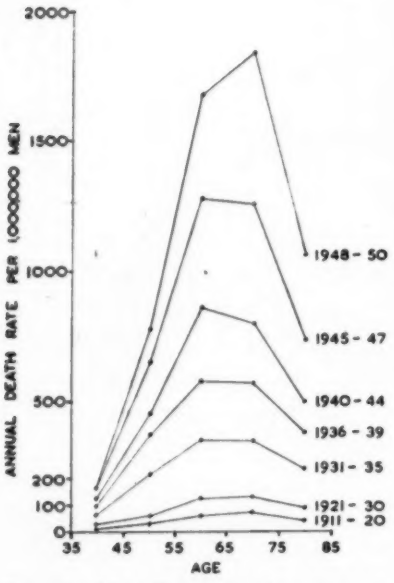

FIG. 1.—Mortality from lung cancer among men at different ages, 1911–50.

Bryson and Spencer's material was collected from the necropsy records of the Central Histological Laboratory of the London County Council over a period when the number of necropsies performed increased rapidly (from 684 to 1,723 a year), although the number of patients admitted to the 26 hospitals concerned fell by a quarter. It seems likely that, in fact, the type of subject coming to necropsy changed considerably, and this is borne out by finding that the proportion of cancers which arose in the large intestine increased from 5% to 13%. If, therefore, Bryson and Spencer's material suggests that bronchial carcinoma did not increase between 1936 and 1947, it also suggests that cancer of the large intestine did—which is contrary to the evidence of mortality statistics and to all clinical impression.

The increase recorded by vital statistics is partly due to the increasing proportion of the population who live to the cancer age. This, however, accounts for only a small part of the increase. If the sex and age distribution of the population in 1950 had been the same as it was in 1931, the general rate for the population would have been 236 per million instead of 278 per million; that is, there would still have been a fivefold increase in 19 years (Fig. 2).

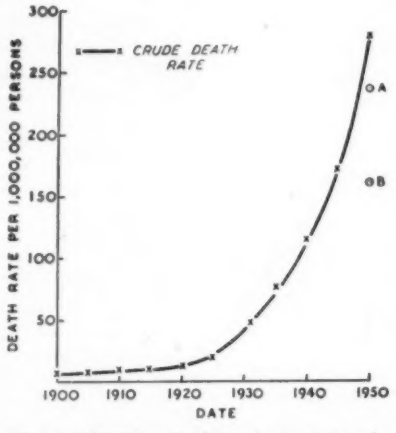

FIG. 2.—Death rate from lung cancer in England and Wales, 1900–50. A = Estimated death rate in 1950 with population of age and sex distribution as in 1931. B = Estimated death rate in 1950 with population of age and sex distribution as in 1901.

It has been held that the great increase in the recorded mortality in Britain may be due to the successive introduction of radiography, bronchoscopy, pneumonectomy, cytological examination of the sputum, and diagnostic thoracotomy. It would indeed be strange if the consequent increased facility in diagnosis had not been reflected in a more general recognition of a clinically obscure disease. It must also be recognized that improvements in therapy of the infectious diseases—particularly of pneumonia—must have reduced the number of deaths occurring from the early complications of lung cancer and so allowed a greater proportion of the cases to proceed to a readily diagnosable stage. In illustration of the close relationship presumed to hold between the lung cancer death rate and the standard of medical diagnosis and certification, Rigdon and Kirchoff (1952) have shown that the correlation coefficient between the death rate and the number of patients per physician in the 48 States of the U.S.A. is −0.66 : that is, the fewer the patients per physician the higher the lung cancer death rate.

In recent years Willis (1948) in Britain and Clemmesen and Busk (1947) in Denmark have, like Steiner (1944) in the U.S.A., expressed the view that the increase is spurious. It seems, however, as pointed out by Heady and Kennaway (1949), that Willis based his opinion on evidence collected before 1933—that is, before the greater part of the increase was recorded, while Clemmesen has revised his opinion (Clemmesen, Nielsen, and Jensen, 1953), and Steiner has been convinced that a real increase has taken place locally—for example, in Los Angeles (Steiner, Butt, and Edmondson, 1950).

Reasons for believing that there has been a real increase are :

(1) The increase in the recorded death rate still continues, despite the long period which has elapsed since attention was drawn to the importance of the disease.

(2) The disease is now so common that had the increase been entirely spurious it would be necessary to postulate that 50 years ago 95% of the fatal cases were wrongly certified.

(3) Necropsy examinations conducted under the supervision of single eminent pathologists, at teaching hospitals where over 90% of the subjects who died came to necropsy—for example, St. Mary's, London, and Leeds General Infirmary — have also shown considerable increases in the proportions of bronchial carcinomas to all cancers and to all necropsies.

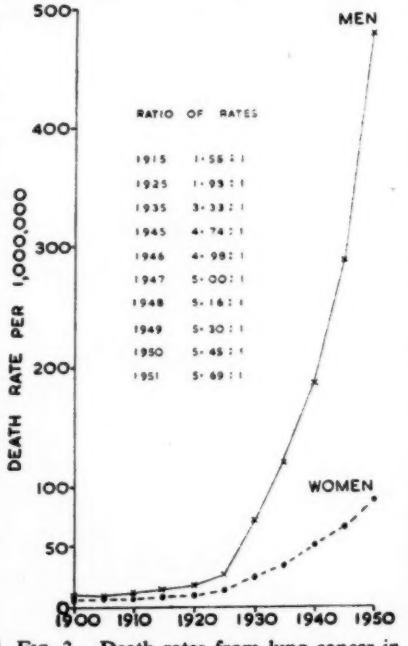

FIG. 3.—Death rates from lung cancer in England and Wales, 1900–50.

(4) The increase has been persistently greater in men. Passey and Holmes (1935) suggested that this might be due to the greater facilities for medical attention available to men under the National Health Insurance Act, but in the few years that have elapsed since the introduction of the National Health Service Act, in July, 1948, the disparity has become even greater (Fig. 3).

(5) The age distribution of lung cancer in men is different from that of all other major types of male cancer, and has been changing in form while its incidence has been increasing. Korteweg (1951) notes that the trends in England and Wales are in conformity with the hypothesis that a real increase has occurred and that successive generations have been exposed to extraneous carcinogens to different extents. The same phenomenon has been observed in Denmark (Clemmesen, Nielsen, and Jensen, 1953).

(6) The death rates in town and country have, in England and Wales, retained the same relation to one another.

(7) The mortality among doctors, who may be presumed to be as carefully investigated as any section of the community, has been practically the same as that for the whole population (Kennaway and Kennaway, 1947; Dublin, Spiegelman, and Leland, 1947).

It cannot be said that all workers are agreed on the conclusions to be drawn; Rigdon and Kirchoff (1952), for example, continue to believe that the increase is wholly spurious. At the International Symposium on the Endemiology of Lung Cancer held last year at Louvain, however, it was agreed that "a significant part of this increase is absolute and represents a real increase in the number of people suffering from cancer of the lung" (Council for International Organizations of Medical Sciences, 1953), and the conclusion of the Symposium seems to me to be reasonable.

How much of the increase is real after standardizing for age and sex remains uncertain. The extent of the change in the last five years, when the importance of the disease has been recognized and facilities for diagnosis have been readily available, suggests that the real increase is likely to be large. I believe it may well be more than half. On the other hand, I would think it certain that some of the increase is nosological and some is due to the therapeutic advance which prevents death from pneumonia before the presence of the underlying growth is evident.

Possible Explanations of the Increase

The importance of the conclusion reached is that it holds out hope for prevention. An increase of the rapidity and extent of that presumed to have occurred cannot be accounted for on the basis of a changing inherent constitution. Some potent environmental factor must have become prevalent, and therefore, when the factor is identified, it may prove possible to reduce its influence.

Factors which have been considered are (1) atmospheric pollution with (*a*) the waste products of domestic chimney and factory smoke, (*b*) the exhaust fumes of vehicles, and (*c*) the dust from tarred roads; (2) the smoking of tobacco; and (3) the after-effects of certain respiratory infections—for example, influenza of the type associated with the 1918–19 pandemic and tuberculosis.

Animal Experiments

The effect of these and other factors has been studied extensively in animals. Unfortunately, although lung tumours have been described in many species, there is no laboratory animal which spontaneously develops tumours comparable to the ordinary squamous or anaplastic carcinoma of the bronchus of man. For example, the common pulmonary tumour of mice, which has been the subject of most experiments, is a papillary adenocarcinoma and, according to Grady and Stewart (1940), is of alveolar rather than of bronchial origin.

Many substances, when fed to mice, painted on the skin, or injected parenterally, increase the incidence of this tumour—the most effective method generally being intravenous injection. Not all strains of mice respond in the same way; strains with high and low incidences of spontaneously occurring pulmonary tumours have been separated and different strains react in different ways to the application of the same substance. Many—though not all—of the hydrocarbons known to be carcinogenic under other conditions have been shown, on testing by these methods, to produce pulmonary tumours. The most potent is urethane.

Tumours more like the human type have been produced in mice by Andervont (1937), by the insertion of a piece of cotton thread impregnated with 1,2,5,6-dibenzanthracene directly into the lungs; by Smith (1950), by the implantation of lung tissue from embryo mice along with solutions containing methylcholanthrene or dibenzanthracene into the thigh muscles of adult animals; and by Lisco and Finkel (1949), by the administration of radioactive cerium (Ce^{144}) in the form of an aerosol.

Substances derived from sources suspected of being implicated in causing human lung cancer have been tested by exposing mice to atmospheres containing the test substance in the form of dust or smoke, or by skin-painting. McDonald and Woodhouse (1942) found an increased incidence of pulmonary tumours in mice exposed to inhalation of soot collected from the air of an English city, and Leiter, Shimkin, and Shear (1942) produced sarcomas in mice at the site of inoculation with extracts of soot collected from the air of several American towns. Campbell (1934) found a greatly increased incidence of pulmonary tumours in mice exposed to an atmosphere heavily laden with the dust from tarred roads, and many animals also developed carcinoma of the skin, presumably from contact with the dust externally; road dust from which the tar had been extracted also increased the incidence of the tumours, but to a less marked extent (Campbell, 1937). Mice kept in an atmosphere of tobacco smoke by Campbell (1936) in Britain and by Lorenz, Stewart, Daniel, and Nelson (1943) in America showed no significant increase in the number of tumours.

In contrast, Essenberg (1952) has recorded an increased incidence in mice exposed to high concentrations of cigarette smoke. The mice came from a strain with a high spontaneous incidence, and tumours were obtained in 21 out of 23 (91%) in the experimental group against 19 out of 32 (60%) in the control group. It may be significant that the cigarette smoke was drawn directly into the animal box in Essenberg's experiment, whereas in the other experiments it was introduced through tubing. In no case have the conditions reproduced those to which men are exposed in smoking, nor can they do so unless animals are trained to smoke. Tar obtained from tobacco burnt at temperatures normally reached in pipe-smoking has resulted in the production of carcinomas when applied to the skin, both in mice (Flory, 1941; Graham, Wynder, and Croninger, 1952) and in rabbits (Sanders, Thomson, Cooper, and Lamb, 1932). The tumours have not been produced easily, but there is no doubt that tobacco tar can contain a carcinogenic agent. Experiments in which animals have been exposed to the exhaust fumes of cars have proved negative (Campbell, 1936; Twort, 1939).

The application of these results to the study of human lung cancer is problematical. In the first place, the pulmonary tumour of mice is histogenetically different from bronchial carcinoma, and tumours which more closely resemble the human type have been produced only by methods which do not appear likely to have any direct counterpart in naturally occurring carcinogenesis. The rarity of bronchial carcinoma in animals accords with the theory that the tumour in man commonly arises from some specifically human activity. In the second place, it is clear that most of the sources suggested as responsible for the production of bronchial carcinoma—atmospheric soot, dust from tarred roads, and tobacco tar—can be shown, by selected methods of application, to contain substances which are carcinogenic for some animals. Whether they are of importance in the production of the human disease can be determined only by observations on man.

Incidence in Different Parts of the World

It is always difficult to compare vital statistics from different countries, and particularly so when they relate to a disease like lung cancer, which is not easy to diagnose with certainty by clinical methods. Necropsy statistics have the advantage that the diagnoses can be relied on, but the populations from which the subjects are drawn are seldom known with accuracy, and much bias may be introduced into the figures, for this reason, without there being any evidence of its nature.

TABLE I.—*Death Rates from Lung, Respiratory, and Non-respiratory Cancers in Various Countries, 1949*

Death Rate per 1,000,000 Non-respiratory Cancer	Country	Death Rate per 1,000,000 Respiratory Cancer	Death Rate per 1,000,000 Lung Cancer	Lung Cancer as % of all Cancers Found at Necropsy
1,584	England and Wales	288	251	31·0, 21·4, 16·1
1,597	Scotland	256	228	20·4
1,086	Finland	171		
1,123	Uruguay	171*		
1,652	Switzerland	151	122	—
1,262	Holland	144	133	16·0
1,545	France	135		
1,256	U.S.A.	131	112	11·3, 10·4
1,474	W. Germany	131		
1,271	New Zealand	127		
1,041	S. Africa	110		
1,131	Canada	106		
1,462	Denmark	106	97	—
1,152	Australia	103		
1,292	Eire	99		
988	Italy	84		
1,407	Iceland	80†	58	3·1
666	Spain	67		
1,411	Norway	63	54	—
809	Chile	47†		

* 1947. † 1948.

Necropsy series.—England and Wales: St. Bartholomew's, 1945–8, St. Mary's, 1945–8, Leeds General Infirmary, 1945–9. Scotland: Western Infirmary, Glasgow, 1945–8. Holland: Amsterdam and Rotterdam, 1951 (Korteweg, personal communication). U.S.A.: Los Angeles, 1943–6 (Steiner, Butt, and Edmondson, 1950); Texas, 1945–9 (Rigdon and Kirchoff, 1951). Iceland: Reykjavik, 1940–50 (Dungal, 1950, and personal communication).

Not all countries which publish vital statistics separate lung cancer from other cancers of the respiratory system. Of those that do, the highest rates recorded in 1949 were in England and Wales (251 per million) and in Scotland (228 per million), the next highest in Holland, Switzerland, and the U.S.A. (all around 110–120), and the lowest in Iceland (58‡) and in Norway (54). Differences of this size (4½ to 1) cannot be accounted for by demographic differences. If, for example, the English rates had held for populations of the sex and age distributions of the U.S.A. and Norway, the death rates would have been 223 and 239 per million and still much higher than the rates actually recorded in those countries.

The forms of respiratory cancer other than cancer of the lung have, in all probability, different aetiologies; lung cancer, however, accounts for such a high proportion of all respiratory cancer that important differences in the mortality from respiratory cancer are likely to simulate underlying differences in the mortality from lung cancer. Figures for the death rate from respiratory cancer are shown in Table I for all those countries for which the statistics are published.

Table I also shows the death rates from all forms of cancer other than respiratory and, for some countries, the death rates from lung cancer alone and the proportion of bronchial carcinomas among all cancers found at necropsy in recent series—that is, in necropsies performed since 1940.

‡The rate for Iceland is for 1948.

The rates for all forms of cancer other than respiratory give an indication of the reliability of the national statistics. All forms of cancer may be relatively infrequent in some countries, but, in view of the great variety of factors responsible for the production of cancer in different sites, conditions favouring a generally low rate are unlikely to be common. A low rate for all non-respiratory cancers in conjunction with the low rate for respiratory cancer must arouse the suspicion that many cases are not diagnosed; a high rate for all non-respiratory cancers with a low respiratory cancer rate will, on the other hand, suggest (though it does not prove) that the respiratory rate is reasonably reliable. If necropsy studies in the same country also indicate a low proportion of lung carcinoma the impression will be strengthened.

With these considerations in mind, it would be unwise to attach importance to the low respiratory cancer rates reported from Italy, Spain, and Chile. On the other hand, in both Norway and Iceland there is no deficiency of diagnosis of cancer generally, and it seems reasonable to believe that the extremely low rates reported for lung cancer are real. In Iceland, moreover, Dungal (1950) found a very low proportion of lung cancers at necropsy at the University Clinic (where necropsy is routinely performed on all patients who die).

Very low incidences at necropsy have been reported from many parts of the world for which vital statistics are lacking (Table II). Gharpure (1948) found no case of lung cancer among 4,321 necropsies performed in Bombay during 1926–46, and Strachan (1934) found none among 1,901 necropsies on native South Africans. In this context, it is of interest that the death rate from lung cancer among the non-white population of the U.S.A. is of the same order as that among the white population, so that the apparent difference found between Europeans and native Africans is unlikely to be due to heredity. The average age at death in the Indian and South African native cases must have been much less than that in recent European series, and this, alone, will have considerably reduced the proportion found to be cancer of the lung. Nevertheless, an appreciable number of cancers were found in the sites which commonly give rise to cancer among Europeans, and it is unlikely that no case of bronchial carcinoma should have occurred in such large series if the condition was as common in India and South Africa as it is in Britain.

TABLE II.—*Incidence of Lung Cancer at Necropsy in Different Countries*

Author	Place	Period	Lung Cancer as % of All Necropsies			Lung Cancer as % of All Cancer Necropsies		
			M	F	M+F	M	F	M+F
—	England (average for St. Mary's, St. Bartholomew's, and Leeds G.I.)	1945–8	6·2	2·6	5·0	29·6	11·0	22·8
See Daff, Doll, and Kennaway (1951)	Turkey (Istanbul)	1945–9	2·8	0·8	2·1	20·3	7·8	17·0
	Yugoslavia (Ljubljana)	1945–9	1·5	0·6	1·1	11·8	3·1	7·1
Shik (1946)	U.S.S.R. (Moscow)	1936–43	—	—	1·8	—	—	15·6
Gharpure (1948)	India (Bombay)	1926–46	0·0	0·0	0·0	0·0	0·0	0·0
Nath and Grewal (1935)	India (Lahore, Lucknow, and Patna)	1914–34	—	—	0·1	—	—	1·5
Kouwenaar (1950)	Indonesia (Chinese)	—	—	—	0·9	—	—	9·2
	Indonesia (Javanese)	—	—	—	0·1	—	—	2·3
Davies (1948)	E. Africa	1931–47	—	—	—	—	—	1·4
Strachan (1934)	S. Africa (Bantus only)	1924–33	0·0	0·0	0·0	0·0	0·0	0·0

Attractive though it may be to conclude that a high death rate from lung cancer reflects principally a high standard of diagnosis, it is probable that real differences in incidence between different parts of the world do exist—particularly between Britain on the one hand and Norway, Iceland, and a number of Asiatic and African countries on the other—even though all of *some* of the recorded differences (and some of *all* of them) may be nosological.

One characteristic, however, is the same for all countries which have recorded vital statistics of lung or respiratory cancer for any length of time. In each one the death rate has increased substantially—even in Norway (Fig. 4).

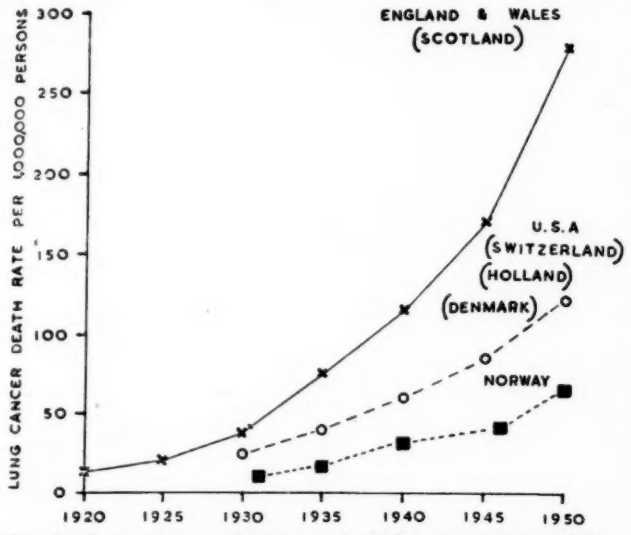

FIG. 4.—Lung cancer. Death rate in different countries, 1920–50. Rates for the countries shown in parentheses were close to the rates for the countries with which they are grouped.

Differences Between Town and Country

Important differences in incidence have also been noted between sections of the population within individual countries. Though mostly less dramatic than the differences between countries, they have hitherto been of greater value in elucidating the aetiology of the disease, since it has been possible to define more precisely the differences in environment to which the separate groups have been exposed. For example, differences in mortality have been noted between countrymen and townsmen and between the inhabitants of towns of different sizes. According to the Registrar-General, the death rate from lung cancer in 1950 was twice as high among the male inhabitants of Greater London as among men living in rural districts, and the difference was more pronounced in the older age group. The rates for other parts of the country fell between the Greater London and rural rates, in exact order of town size (Fig. 5). Female rates show the same trends, though the differences are less marked and the trends somewhat blurred, possibly owing to smaller numbers. Comparison of the relative differences at different periods shows that these differences have remained remarkably stable despite the great increase in the recorded mortalities.

Stocks (1952) has analysed the urban death rates for the period 1946–9 and has demonstrated a progressive increase with the increase in the number of inhabited houses. Within Greater London, he found that the boroughs with the highest mortalities were situated to the north and east of the town's centre. This, he suggests, may be related to the direction of the prevailing wind, which is from the south-west—and might therefore be expected to shift the area of maximum smoke density to just that part of the town in which the highest mortalities occur.

As always, when drawing conclusions from vital statistics, it must be asked whether the differences can be purely nosological; whether the "factor" is nothing more than a greater facility for diagnosis in the larger towns. This seems unlikely. In the first place, it would hardly be expected that diagnostic acumen should be so closely dependent upon the exact size of town; secondly, there is the stability of the urban : rural ratio; and, thirdly, there is direct evidence obtained by Doll and Hill (1952). They found, among 1,465 patients with carcinoma of the lung and the same number of matched control patients with other diseases, that the proportion who had ever lived for any long period in the country was lower among the carcinoma patients, irrespective of their present place of residence. That is to say, among patients residing in Greater London at the time of interview a lower proportion of those with lung carcinoma than of those with other diseases had ever lived for 10 or more years in a rural district—and similarly for each other place of present residence. The differences were small and not statistically significant, but they were all in the same direction, and provide some support for the belief that the risk of developing lung cancer is, in fact, lower in the countryside.

The observation of a town and country difference is not confined to Britain. Clemmesen, Nielsen, and Jensen (1953) have reported an even more pronounced difference between the capital and rural areas of Denmark. In their opinion, however, the difference is not constant, but may be explained by the spread of a new carcinogenic factor to the countryside, 10 years after it had begun spreading in the capital.

In Norway, the difference between urban and rural areas—as definite as in Britain, despite the low total incidence—is also increasing. Mortality statistics, for which I am grateful to Professor Kreyberg, provide the following comparisons:

Ratio of Death Rate in Town and in Country

	1931–5	1946–50
Men	1·8 : 1	2·5 : 1
Women	1·1 : 1	1·5 : 1

It seems, therefore, as if differences are constantly in the same direction, but that there may also be local differences which modify the trends in different countries.

Three substances known to be carcinogenic under suitable conditions have been identified in town air. According to Dawson (1952) radioactive material is present to the extent of $30–100 \times 10^{-12}$ curie per m.^{3} Activity in the open air of towns is not much greater than in rural areas, but within closed rooms the activity may be doubled, and in extreme cases, as in an underground shelter, it was found to be 100 times greater. Even this value is, however, only one-tenth of the tolerance concentration—unless it proves (as it may do) that the limit at present accepted is set too high.

The amount of arsenic varies, according to Goulden, Kennaway, and Urquhart (1952), from 0.04 μg. of As_2O_3 per m.^{3} in Bristol to 0.16 μg. per m.^{3} at Beckton, in London.

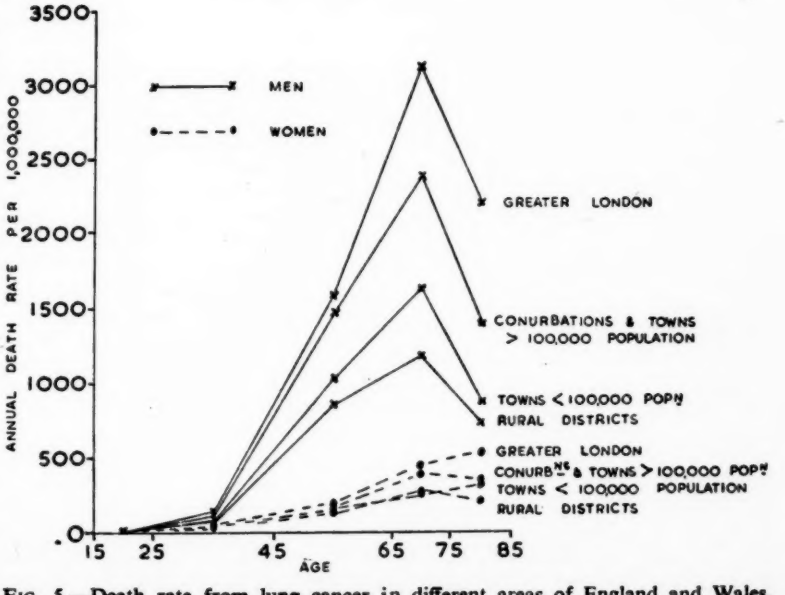

FIG. 5.—Death rate from lung cancer in different areas of England and Wales, 1950.

It is, however, difficult to ascribe any one value to a town, as there are considerable variations between stations within towns—for example, the concentration in the air at County Hall, London, was only a third of that found at Beckton and only slightly greater than that recorded in Bristol. The total amount inspired by a town dweller per year is estimated by Kennaway to be 0.5 mg., which is only one-tenth of the amount in the maximum official dose of Fowler's solution (0.5 ml.).

According to Waller (1952), benzpyrene is present in town air, in amounts varying from 0.013 μg. per m.^{3} in Bristol to 0.046 μg. per m.^{3} of air in the centre of London. Again, however, variations in the concentration make it necessary for many readings to be obtained before a fair estimate can be made of the content of the air of a town as a whole. Winter concentrations are three to four times greater than summer concentrations, and great increases are obtained during fogs. In Waller's opinion the variations in benzpyrene content suggest that most of it is derived from the smoke of domestic fires. Some has, however, been detected in motor exhausts, and, since the sizes of the particles in exhaust smoke are concentrated over a limited range of small sizes, this source could be of greater biological significance than appears from the proportion which it contributes to the total air pollution.

Occupational Risks

The classical method leading to the isolation of chemically pure carcinogens is the observation of specially high cancer risks in specific occupations. With lung cancer, exceptional risks have been recognized in several unrelated industries. These are: mining of various ores in Schneeberg (Germany) and in Jachymov (Czechoslovakia); chromate production; nickel-refining (in Clydach, S. Wales); asbestos manufacture; and the production of gas. To these should probably be added the handling of inorganic arsenic and, possibly, occupations providing excessive exposure to iron dust, with or without added exposure to silica.

The risks involved have been estimated only for chromate workers and gas-workers. Brinton, Frasier, and Koven (1952), extending the initial observations of Machle and Gregorius (1948), have compared the sickness and mortality experience of insured workers in the seven chromate-producing plants in the U.S.A. with the whole sickness data obtained by the U.S. Public Health Service and the death rates for the U.S. population. They found that the mortality from lung cancer among white males employed in the plants was 14 times the expected, and among coloured males it was 80 times the expected. According to Bidstrup (1951) the risk is unlikely to be as great in the British chromate industry.

Doll (1952) studied the causes of death among 2,071 male pensioners of a London gas company and found that the number of deaths from lung cancer was approximately double that expected by comparison with male inhabitants of London of the same age distribution—that is, 25 deaths against 13.8. Confidence that this small excess is real derives from the observation that for all other causes of death studied the numbers observed were not significantly different from those expected; it is also of the same order as that determined by Kennaway and Kennaway (1947), when they drew attention to the possibility of there being a risk in the gas industry.

Of the other occupational risks, that incurred in the Schneeberg and Jachymov mines is likely to have been the highest: as much as 50 to 75% of all deaths among the miners may have been due to lung cancer (Haerting and Hesse, 1879; Lange, 1935; Peller, 1939). The risk in the Clydach nickel refinery—at least till the reorganization of the plant in 1924—must also have been considerable (Chief Inspector of Factories, 1949). In the manufacture of asbestos and arsenical sheep dip the risk is more likely to have been of the same order as that involved in the production of gas. For example, Gloyne (1951) found that of 52 men dying with asbestosis, about 20% gave evidence of the presence of a primary lung cancer, whereas among men with other forms of pneumoconiosis the proportion was 7%. As is shown later, there are reasons for believing that the incidence among men with pneumoconiosis is generally close to the average.

The evidence of the existence of a risk of lung cancer in the handling of inorganic arsenic derives from an investigation by Hill and Faning (1948) into the causes of death among men employed in a factory making sheep-dip. They traced five deaths due to lung cancer among these men, whereas they estimated, by comparison with the causes of death in other workers in the area, that there should have been only one.

The existence of special cancer risks in most of these industries is not surprising, since the workers in them have been exposed in the past (and in some cases still are exposed) to unusual concentrations of known carcinogens. According to Evans (1950) the mean concentration of radon in the air of the Jachymov mines is about 3×10^{-4} curie per m.^{3}, while the tolerance concentration is at the most 10^{-7} curie per m.^{3}—that is, one-thirtieth of that found in the mines. Hueper (1952) has produced sarcomas in mice at the site of injection with suspensions of finely dispersed nickel powder, and nickel must be presumed to be deposited in the respiratory passages on the decomposition of nickel carbonyl, a gas produced in the refining process at Clydach. Gas-workers are exposed to coal tar—one of the most prolific sources of carcinogenic hydrocarbons and including benzpyrene. Finally, arsenic is known to produce cancer of the skin in man when ingested over long periods, and large quantities (up to 1,000 μg. per m.^{3}) were found in the atmosphere of the sheep-dip factory (Perry, Bowler, Buckell, Druett, and Schilling, 1948).

No direct evidence is available on the nature of the carcinogenic factor in the chromate and asbestos industries.

The position with regard to iron-workers is obscure. Turner and Grace (1938) found that foundry-workers, smiths, and metal-grinders had a mortality from lung cancer higher than that of any other occupational group in Sheffield; and Turner and Martin (1949) found that out of 32 cancer deaths among grinders with silicosis the lung was the primary site in 19. Metal-grinders also suffered a high mortality from lung cancer in Kennaway and Kennaway's (1947) material. These observations might be thought to imply that silicosis predisposed to lung cancer, but this has been convincingly shown not to be true (Miners' Phthisis Medical Bureau, 1936; Kennaway and Kennaway, 1947). If there is any excess among special groups of metal workers it must be presumed to be due to some other, and more specific, industrial hazard.

An attempt has been made to discover whether any other common occupation carries a special risk by interrogating patients with and without bronchial carcinoma about their past occupations. The questions were asked as part of a general investigation into the aetiology of bronchial carcinoma which has been described previously (Doll and Hill, 1950, 1952). Altogether 1,357 men with bronchial carcinoma and 1,357 men with other diseases were interviewed. Occupations in which the men had been employed for three or more years were recorded; no account was taken of time spent in the Services unless the patient had served as a regular, and no analysis was made of employments under the age of 20, when changes of occupation were frequent. Many men had worked in two or more occupations for the minimum of three years, so that the number of occupations recorded was greater than the number of men interviewed—2,281 for the men with lung carcinoma and 2,415 for the same number of men with other diseases. Of all the 76 groups into which the occupations were classified, there were only two in which the differences between the numbers of

bronchial carcinoma and of control patients who had been employed in them could be considered, by the usual statistical criteria, to be significant. The occupations recorded of the bronchial carcinoma patients included 80 in coal-mines and 16 in the police forces; of the control patients, there were 113 in coal-mines and 32 in the police forces. In view of its correspondence with the results of the analysis of the national mortality data made by Kennaway and Kennaway (1947), the deficiency of coal-miners among the bronchial carcinoma group may reasonably be taken to confirm that coal-miners are subject to a lower incidence of bronchial carcinoma than other industrial groups. The deficiency in the cancer group of men who had been employed as policemen may, in the absence of other evidence, be attributed to chance, since there is nothing surprising in finding one difference of this extent when so many groups have been studied.

The most important excess in the cancer group occurred in men who had been directly concerned with the production of gas; the cancer group contained 23 such men, the control group 14. Other evidence has shown that gas-workers are exposed to a special risk of lung cancer, and the present figures are corroborative—although, by themselves, not statistically significant.

The closeness of the numbers in the two disease groups who had been employed in many of the other occupations is striking. This is particularly so for occupations which might have been expected to be disproportionately represented in the lung-carcinoma group, if exposure to the dust of tarred roads or to motor exhaust fumes was responsible for many cases of the disease.

	Men with: Lung Carcinoma	Other Diseases
Motor mechanics, garage hands	19	25
Drivers of cars, lorries, or buses	105	101
Bus and tram conductors	10	21
Van drivers (horse)	33	25
Other road transport	17	25
Roadmen, council labourers, dustmen	39	39

The failure to find any difference in the relative proportions of men employed on the roads or in the service of cars is of interest. It accords with the conclusion of Kennaway and Kennaway (1947) that none of the open-air occupations, where there was special exposure to road dust, had a high incidence of cancer of the lung.

The results provide little or no support for the suggestion of Wynder and Graham (1951) that painters and what they describe as "hot" metal workers may suffer special risks.

	Men with: Lung Carcinoma	Other Diseases
Painters and decorators	70	59
Furnacemen, foundrymen, and smiths	26	23
Other metal workers	150	157

The evidence from a study of occupational factors is therefore that the development of bronchial carcinoma may result from prolonged exposure to a number of atmospheric carcinogens; some of these substances, like radon, benzpyrene, and arsenic, are present in town air—though in very much lower concentrations than occur in industry; others, like nickel, are peculiar to specialized industrial processes; others are as yet undetermined. So far as it goes, the evidence is against the hypothesis that motor fumes and road dust are responsible agents.

Although one occupation—the refining of nickel—is also responsible for a high incidence of cancer of the nasal sinuses, it is a remarkable fact that none of the occupations known to be associated with a high incidence of lung cancer appears to carry any increased risk of laryngeal cancer. It is probable, therefore, that the factors which are responsible for the production of carcinoma of the bronchus and for carcinoma of the larynx are independent.

Sex Ratio

According to all reports the incidence of lung cancer is much greater in men than in women. The extent of the difference is, however, uncertain. In this country the mortality statistics of the Registrar-General gave, in 1950, a ratio of 5.2 male deaths to every female death, and the proportion has been increasing steadily, though slowly, from year to year. During the first half of 1949 Mackay's (1951) study of in-patients discharged from a number of selected hospitals (mainly teaching hospitals) gave a ratio of 5.1 to 1 and the national cancer registration scheme (which is believed to cover about half the cases in the country) gave, in 1946, a ratio of 6.9 to 1 (Stocks, 1950). Much higher ratios have been recorded in recent clinical series—varying from 7.3 to 1 to 12.6 to 1 (Fulton, 1949; Mason, 1949; Brooks, Davidson, Thomas, Robson, and Smithers, 1951; Doll and Hill, 1952).

The inconsistency may be partly due to the inclusion of a proportion of inaccurately diagnosed cases in the national

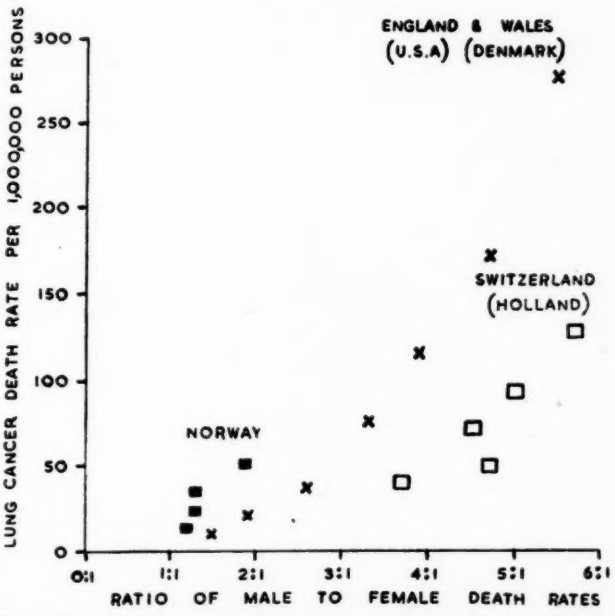

FIG. 6.—Lung cancer. Ratio of male : female death rates at different levels of incidence in different countries. Ratios for the countries shown in parentheses were at each level of incidence similar to the ratios for the countries with which they are grouped.

figures (though this should not apply to the cancer registration scheme), but it may also be due to the process of selection, which to some extent accompanies the collection of any clinical series—for example, through the exclusion of out-patients, the relative exclusion of the very old, or the availability of male and female beds.

Experience of the full and accurate registration scheme which is now operating in Denmark suggests that the true ratio is probably somewhat—though not much—higher than that indicated by death certificates, and it is reasonable to believe that the true ratio in the United Kingdom is, at the present time, of the order of 6 or 7 to 1.

At the beginning of the century the sex ratio, judged by mortality data, was as low as 1.3 to 1. In Norway the ratio is to this day not much greater. Generally it would appear that in all countries the higher the incidence of the disease the greater the male preponderance (see Fig. 6). It is notable that the relation between the sex ratio and the total incidence is not the same in all countries, but that in some a given degree of male preponderance is reached at a lower general level of incidence. It seems probable, therefore, that the factor mainly responsible for the increase is one to which men are particularly exposed and that the extent of the relative difference in exposure of men and women varies from country to country.

(Part II will appear next week with list of references).

SOME APPARENT ANOMALIES OF POTASSIUM METABOLISM

BY

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The importance of potassium in the body economy has for long been a matter of interest only to the physiologist. Within recent years, however, the recognition of serious potassium depletion in clinical conditions has aroused interest in potassium metabolism in health and disease. Our knowledge of this important cation has been derived from a wide variety of experimental and clinical observations, and the time seems ripe for a brief summary of the more important contributions.

Potassium Deficiency

In 1915 Benedict showed that potassium was lost along with nitrogen in fasting states, and, later, similar observations of potassium loss in diarrhoea (Butler *et al.*, 1933) and in diabetic coma (Atchley *et al.*, 1933) were made. The relationship of potassium to muscle contraction and muscle metabolism has always been of interest. In 1936 Brown and Feldberg showed that potassium liberated acetylcholine at ganglionic synapses. Fenn and Cobb (1936) found that, after indirect stimulation of the muscles of anaesthetized rats, potassium was lost from the muscle cell in exchange for sodium. These changes were reversed after rest, indicating that no irreversible damage had been done to the muscle. Cuthbertson *et al.* (1939) showed that, following operative fracture of the femur in rats, large amounts of potassium were lost in the urine, associated with an increased excretion of nitrogen and phosphorus. They observed that the potassium loss was relatively greater than the nitrogen loss, and seemed to be far greater than could be accounted for by the local changes at the site of injury.

The observations of Mullins *et al.* (1941) on the sodium permeability of the red cell indicated that the older concept of the impermeability of the cell to the cation sodium was not correct. Miller and Darrow (1941) showed that deoxycortone acetate reduced the muscle potassium content of rats and increased the muscle sodium content. This exchange of sodium for potassium in the cell was also demonstrated by Heppel (1939) and Miller and Darrow (1940a) in animals fed on a low-potassium/high-sodium diet. It was later observed in some clinical conditions such as alkalosis (Gamble *et al.*, 1945 ; Darrow, 1945), and in some types of infantile diarrhoea (Darrow, 1946).

By this time the loss of potassium in clinical conditions, often associated with signs of paralysis, had become recognized. Brown *et al.* (1944) observed a low serum potassium in chronic nephritis, associated with attacks of paralysis. Similar paralysis as a result of diminished extracellular potassium was described by Holler (1946) in treated diabetic coma. Govan and Darrow (1946) reported large losses of potassium in infantile diarrhoea, and observed that treatment with potassium improved the clinical state. In the development of hypokalaemia during the treatment of diabetic acidosis, Greenman *et al.* (1949) suggested that the dilution of extracellular potassium by intravenous infusions, the continued loss of potassium in the urine, and the migration of potassium from the extracellular to the cellular phase might all contribute to the final clinical picture.

Potassium loss has also been observed after saline infusions (Stewart and Rourke, 1942 ; Gamble, 1942), after major surgical operations (Blixenkron-Møller, 1949 ; Wilkinson *et al.*, 1950), in *p*-aminosalicylic acid therapy, using the sodium salt (Cayley, 1950), in the use of ion-exchange resins (Dock and Frank, 1950), in idiopathic steatorrhoea (Lubran and McAllen, 1951), in pyloric stenosis (Hawkins *et al.*, 1951), and in chronic nephritis (Davidsen *et al.*, 1951). It seems probable that the potassium loss in such widely divergent conditions may be due to a few factors common to many clinical states. No matter the cause, the symptoms of hypokalaemia in all these conditions are similar, and are well summarized by Darrow and Pratt (1950) : (1) weakness and hypotonia of skeletal muscle, leading finally to paralysis ; (2) dyspnoea with gasping respirations ; (3) cyanosis, chiefly respiratory in origin ; (4) abdominal distension ; (5) nausea and vomiting ; (6) cardiac enlargement with systolic murmurs ; (7) increased pulse pressure with Corrigan pulse ; (8) elevated venous pressure with signs of cardiac failure ; and (9) electrocardiographic changes.

Many of these signs of potassium deficiency are common to deficiencies of other electrolytes and of water, and are not, therefore, always convincing evidence of potassium lack. This matter is considered later, but it is important to appreciate that the electrocardiographic changes can be of considerable aid in diagnosis. These changes have been studied carefully by Frenkel *et al.* (1947), Nadler *et al.* (1948), and by Tarail (1948), and they have correlated the following changes with progressive deficiencies of potassium in the serum : (1) prolonged Q–T interval ; (2) decreased height or inversion of the T wave ; (3) rounded and prolonged T wave ; (4) depression of the ST segment ; and (5) inversion of the P wave, extrasystoles, and heart-block.

Hyperkalaemia

The toxic effects of increments in the extracellular potassium have also been widely studied. Hyperkalaemia is a danger only in renal failure and after the injection or absorption of potassium salts. Miller and Darrow (1940b) observed that the toxic effects of injected potassium salts in experimental conditions are directly related to the increase in concentration of that cation in the serum, and only indirectly to the muscle potassium content. This was confirmed in cats by Crismon *et al.* (1943). Folk *et al.* (1948) confirmed that the serum potassium content accurately reflects the potassium content of the extracellular fluids. The effects of increments in the extracellular potassium were studied by Winkler *et al.* (1938). They showed that, in dogs, the electrocardiographic changes due to the toxic effects of extracellular potassium could be directly correlated with the serum potassium concentrations. Briefly they noted: (1) increased amplitude and reduced duration of the T wave regularly appeared at concentrations of 5–7 mM of potassium per litre ; (2) depression of the ST segment at 8–10 mM per litre ; and (3) intraventricular block began at concentrations of 10 mM per litre, the P wave disappearing at 9–11 mM per litre, and cardiac arrest ensued at 14–16 mM per litre.

By depleting the muscle potassium, Miller and Darrow (1940a, 1941) were able to show that rats could be made resistant to the toxic effects of injected potassium salts. They concluded that this depletion of cell potassium enabled this cation, when injected in excess, to enter the cell, thereby protecting the extracellular fluid from a lethal rise in concentration.

Normally the kidney prevents toxic increases in the potassium concentration in the extracellular fluid. The excretion of potassium, as indicated by Smith (1951), is complicated. Potassium reabsorption occurs in the proximal tubule, but it has been necessary to postulate tubular excretion in the distal system, and this, though normally slight, is increased in all conditions of increased extracellular potassium. As Smith points out, this is the first instance in which experimental evidence has made it necessary to postulate the simultaneous reabsorption and excretion of any substance by the kidney tubules. Durlacher and Darrow (1942) showed that the life of nephrectomized animals could be prolonged by procedures which had previously depleted the body potassium stores. They concluded that the mechanism of this prolonged survival was therefore due to the delay in the post-operative rise in the serum potassium. These experiments were in agreement with the clinical data already available, indicating that some of the toxic effects in renal insufficiency were due to an increase in the serum potassium concentration (Winternitz *et al.*, 1940; Addis and Lew, 1939).

The purpose of this paper is to attempt some correlation of these various facts about potassium exchanges in clinical conditions and to analyse the means of diagnosis at our disposal.

Clinical States of Potassium Deficiency

Deficiency may be induced by prolonged reduction in intake or by abnormal loss. In many conditions, such as surgical operation, diarrhoea, and pyloric stenosis, both these factors are operative, and hasten the onset of the condition. As has been indicated above, the work of Benedict and later observers has shown that the protein catabolism associated with starvation also increases the loss of potassium from the body.

The loss of body fluids containing potassium may also hasten the onset of potassium deficiency. Gastric juice contains about 16 mEq of potassium per litre as well as hydrochloric acid. The starvation associated with pyloric stenosis, resulting in diminished intake, increased urinary output, and potassium loss by vomiting is a good example of the forces acting to precipitate potassium deficiency. If, in addition, saline infusion is liberally used in treatment it is hardly surprising that symptoms of potassium lack become manifest. Deficient intake, loss by the gastrointestinal tract either as stomach contents or diarrhoea fluid, and excessive loss during starvation can all be readily understood, and measures can be taken to estimate the potassium loss and to employ replacement therapy. It is with the urinary potassium loss that we are particularly concerned here.

Tarail and Elkinton (1949) have shown that, even in deficiency states, the kidney appears to have a limited minimal excretion of potassium. Unlike sodium, therefore, the kidney seems unable to conserve potassium when it is most required. This continued excretion in the urine in a patient already depleted of potassium is an important factor in producing severe deficiency. It has also been shown that a major surgical operation markedly increases the excretion of potassium in the urine (Blixenkrone-Møller, 1949; Wilkinson *et al.*, 1950). These writers have also shown that the phase of increased potassium excretion can be detected earlier than the phase of protein catabolism, and that the potassium loss is greater in proportion than the nitrogen loss. These effects are very similar to the experimental observations of Cuthbertson *et al.* (1939) on trauma in rats.

I have shown that this urinary potassium loss occurs also in the first three days after relatively minor operations such as interval appendicectomy and inguinal herniorrhaphy (MacPhee, 1952). In this series of patients the blood loss was minimal, hydration was adequate, and intravenous saline infusion was not necessary, thereby preventing the potassium loss shown by Gamble (1942) to result from such treatment. This potassium loss may amount to as much as the equivalent of 10 g. of potassium chloride in the first three post-operative days. As a result of these observations and the associated sodium, chloride, and water retention, the eosinopenia, the increased 17-ketosteroid excretion, and the elevation in blood sugar in these patients, I have suggested that the electrolyte changes are the result of increased adrenocortical activity. It is probable that, provided the adrenal cortex is functioning, these metabolic changes are the natural response of the body to trauma. Such observations are in accord with the well-known hypothesis of Selye (1950), and, as he suggests, may occur in a wide variety of disease conditions and "stresses."

It is too early yet to say whether the increased potassium loss in such conditions as diabetic coma and other acute medical conditions is due to this "stress response" or not. Gamble (1942) has suggested from the work of Darrow that, in conditions of extracellular dehydration (as in infantile diarrhoea), potassium along with water is withdrawn from the cell. Wilkinson *et al.* (1950) suggest some similar mechanism to account for the increased potassium excretion after major surgical procedures. As I have indicated, however, this does not seem to be the operative mechanism in minor surgical trauma, as no appreciable changes were detected in the plasma volume or extracellular fluid space volume, and slight increases were detected in body weight, indicating water retention in the body. Further evidence in favour of the stress mechanism in acute medical conditions has been obtained by Prunty (1949), who observed evidence of increased adrenocortical activity in acute porphyria.

Diagnosis

Although there is no complete agreement on the mechanism leading to urinary loss of potassium in these widely disconnected conditions, the fact that potassium deficiency may supervene is now well recognized. The diagnosis of incipient potassium deficiency, however, remains difficult. The reasons for this have not been made clear. Apart from the electrocardiographic evidence, the signs and symptoms detailed above are often similar to the disease initiating the potassium loss. In addition, sodium chloride and water lack may precipitate cyanosis, abdominal distension, and peripheral circulatory failure, and must be considered as factors in addition to the concomitant potassium deficiency.

Concentrations of potassium in the serum below 3.5 mEq per litre are generally thought to indicate a deficiency of the cation. It is not generally appreciated, however, that the serum potassium concentration may be essentially normal when there is considerable cellular potassium depletion. I have now seen on several occasions electrocardiographic evidence of potassium deficiency associated with a "negative" potassium balance in the presence of a normal extracellular potassium concentration. Danowski *et al.* (1949), in accurate balance experiments, have shown that positive cell balances of potassium were recorded in patients who had normal serum levels of the ion. In the clinical experiments previously noted I have shown that the post-operative serum potassium concentration did not fall below 4.5 mEq per litre in my series, although a large increase had occurred in the urinary excretion of potassium. Frequently, indeed, the serum potassium was observed to rise during this phase. I believe this indicates that potassium is derived from the cells in the post-operative phase as rapidly as, or even more rapidly than, it is excreted by the kidney. This would account for the apparently anomalous findings of potassium deficiency in the presence of a normal or near-normal serum concentration of the ion.

In view of these observations and the experimental records cited above, it may be said that, in the early stages at least, the symptoms of potassium depletion are due to a reduction in the intracellular potassium and not in the serum potassium. It is therefore unwise to wait for biochemical evidence of potassium depletion in the serum before

considering potassium deficiency. Provided renal function is adequate, potassium deficiency must be *expected* in all patients who have undergone major surgical procedures, especially if oral feeding is not possible by the fourth post-operative day; if deficient potassium intake has occurred before operation; if potassium loss is augmented by vomiting, diarrhoea, dehydration, or saline infusion; and if potassium is not supplied at least in maintenance doses. If oral feeding is not possible the potassium loss in the urine, intestinal aspiration, and diarrhoea fluid should be estimated, and the appropriate quantity of potassium supplied.

One further point in regard to potassium deficiency needs to be mentioned. Low concentrations of serum potassium have recently been recorded in association with paralytic ileus. Streeten and Ward-McQuaid (1952) have published observations on this subject, but were unable to prove conclusively that paralytic ileus is always due to serum potassium deficiency. The paralytic ileus which results immediately on the perforation of a peptic ulcer is not associated with a serum potassium deficiency and it seems improbable that this should be the case. (In the absence of other evidence, a reflex "neurogenic" basis must be postulated.) Such a condition, if untreated, is rapidly followed by peripheral circulatory insufficiency due to sodium chloride deficiency which itself increases the ileus (Streeten and Williams, 1952). In the early stages such an ileus will recover rapidly after saline infusion. If, however, the ileus is allowed to persist untreated, the intestinal aspirations and the frequently associated operation may precipitate a potassium deficiency which will increase the tendency to ileus.

The fact that the early stages of potassium deficiency are not necessarily associated with a low level of serum potassium indicates that some method of determining the cellular potassium concentration is required. Electrocardiographic evidence is helpful. In the study of potassium loss after operation associated with normal serum potassium concentration I attempted to measure the erythrocyte potassium concentration (MacPhee, 1952). By estimating the serum potassium and the potassium content of lysed blood, and by utilizing haematocrit readings, the red-cell content can be measured. Although able to detect increases in the erythrocyte sodium immediately after operation, no constant changes were observed in the erythrocyte potassium. Such studies, though pursued in only a small series, seem to indicate that the erythrocyte potassium cannot be satisfactorily used as an index of muscle potassium content.

Treatment of Potassium Deficiency

Potassium deficiency states exist usually with deficiencies of other ions, and the object of treatment is to correct the total ionic imbalance rather than to correct any particular deficit. Any discussion of potassium replacement therapy alone must therefore, of necessity, be brief, and in general terms only.

If an adequate diet containing meat and vegetables can be taken there is little need to supply potassium by other means. If possible it is best to supply any potassium deficit by mouth, thereby allowing absorption as required and preventing a too rapid rise in the extracellular potassium concentration. Serious potassium deficiency, however, usually arises in cases in which oral feeding and therapy are not possible.

Elkinton and Tarail (1950) have estimated that the usual potassium deficiency encountered in the adult may vary from 228 to 936 mEq, roughly about 8–36 g. of potassium. They suggest that, if replacement therapy is to be undertaken by the intravenous route, no more than 20mEq of potassium per hour in a solution with a maximum strength of 80 mEq per litre should be administered. As an example, a solution containing 4.5 g. of the monohydrogen phosphate (K_2HPO_4) and 1 g. of the dihydrogen phosphate (KH_2PO_4) added to a litre of water supplies 60 mEq of potassium per litre. In severe deficiency states 250 ml. of this solution may be supplied each hour, provided adequate means of checking the serum potassium concentration are available.

A chloride deficiency in association with the potassium deficiency is often present in pyloric stenosis. In such cases potassium chloride (KCl) provides a suitable means of rectifying the cation and some of the anion deficiency. Each gramme of potassium chloride contains 13.4 mEq of potassium.

If the potassium deficiency is associated with severe sodium depletion, as in prolonged vomiting of intestinal contents, Darrow's solution provides a suitable method of treatment. This "K-lactate" solution contains 4 g. of sodium chloride, 2.7 g. of potassium chloride, and 52 ml. of molar sodium lactate per litre. The solution can be given in a four-hour period, but, as the potassium concentration is about ten times that of the serum, it is safer to prolong the administration over a somewhat longer interval.

It will be readily appreciated that the parenteral therapy outlined above cannot be followed unless renal function is adequate and unless the concentration of potassium in the serum can be rapidly estimated as treatment progresses.

Increased Extracellular Potassium

Unlike the effects of potassium deficiency, the toxic effects of increased body potassium are usually related to the extracellular concentration of the ion. As already indicated, the toxic effects can be correlated directly with the serum potassium concentration. As a result, the curious anomaly of potassium intoxication may occur during the treatment of cellular potassium deficiency. I have seen a case of pyloric stenosis in the late post-operative period complicated by paralytic ileus, and with an initial serum potassium concentration of 3.5 mEq per litre, showing signs of potassium intoxication as a result of too rapid parenteral replacement therapy.

In clinical practice increased concentration of potassium in the serum is encountered mainly in states of renal insufficiency and in oligaemic shock.

Anuria and Severe Oliguria

The experimental work on this subject has already been considered. In spite of the experimental evidence obtained by Durlacher and Darrow (1942), they did not believe that fatal increases in concentration in the extracellular potassium were the cause of death in anuria. In association with Winkler *et al.* (1938) they thought that the symptoms of potassium intoxication were totally different from those of uraemia.

The cause of the increase in extracellular potassium is an interesting problem. An exogenous source can be excluded, because the rise in the serum potassium can be observed when such patients are starved. Elkinton *et al.* (1949) showed that the rise in extracellular concentration was derived mainly from intracellular potassium. It has been assumed that this increase in extracellular potassium in the anuria associated with mismatched transfusion results from haemolysis and the liberation of potassium from the red cells. There are many objections to such a theory. The rise in serum potassium is rarely noticeable in the first day

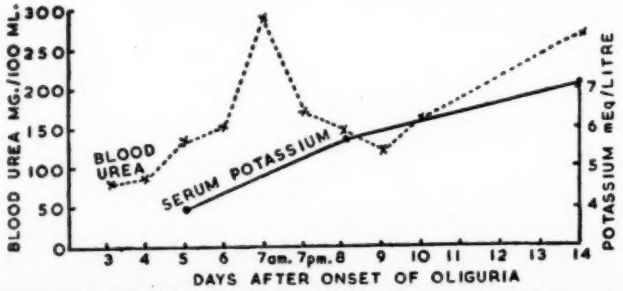

Chart showing effect of peritoneal dialysis on blood urea and serum potassium concentration in patient with severe oliguria.

or two after the transfusion. The Chart demonstrates this point in such a case, and shows that the rise is progressive in the later stages. The Chart also illustrates the effect of peritoneal dialysis in reducing the blood urea, but not in reducing the serum potassium concentration when a solution such as Ringer's is used as the dialysate. It is also interesting to note that the patient remained clinically well, though suffering from severe oliguria, until the eighth day, when symptoms of uraemia began to appear. At this time the blood urea concentration had been greatly reduced by dialysis, the carbon dioxide combining-power of the plasma had returned to 60 volumes%, and the plasma chlorides had risen to 82 mEq per litre. Though this is not direct evidence of potassium intoxication, the uraemic symptoms were certainly associated with the increase in the serum potassium. When recovery ensued after thirteen days' oliguria, the serum potassium rapidly returned to normal.

In view of the fact that the rise in extracellular potassium in such states is a progressive one, I believe that increased adrenocortical activity may be the cause of the potassium withdrawal from the cells. The "stress" origin of such a cell depletion would be in line with the mobilization of potassium from the cells after trauma, operation, and other tissue injuries. There is as yet, however, no real proof of this mechanism. The gradual rise in the serum potassium could be explained in other ways. For example, after crush injuries much potassium may be liberated from the damaged muscle. Potassium may also be derived from the cells during the protein catabolism of starvation. The mechanism therefore remains in doubt.

Treatment

Kolff (1950) has shown that *subnormal* serum potassium concentrations may actually be produced in uraemia in patients on a Borst diet (high carbohydrate, low protein). Fenn (1939) showed that potassium is deposited in the liver along with glycogen. Experimental evidence suggests therefore that after injections of carbohydrate a movement of potassium from the extracellular to the intracellular spaces takes place. This may be a part of the merit of a treatment such as that of Bull *et al.* (1949), in which a high carbohydrate intake is advocated.

If the extracellular potassium concentration has already reached toxic levels before adequate treatment is begun, some form of dialysis may be necessary. Intestinal dialysis as described by Black and Stanbury (1948) is a most suitable method of reducing the extracellular potassium concentration in such cases. Peritoneal dialysis is cumbersome, and may be dangerous.

Summary

Potassium deficiency may occur as a result of deprivation of the ion, by excessive loss though vomiting, by diarrhoea, or in the urine.

The loss is accentuated by saline infusion, operation, injury, and perhaps by other stress conditions.

The symptoms of potassium deficiency may occur when the serum potassium concentration is still within the normal range. The symptoms are therefore due to cellular potassium depletion.

The erythrocyte potassium concentration is not an index of the muscle-cell potassium content.

Symptoms of potassium intoxication are directly related to the extracellular potassium concentration, and not to the cell potassium content.

ADDENDUM.—In the recovering phase of renal cortical necrosis when diuresis ensues, it has always been our experience that excess potassium is rapidly cleared from the extracellular fluid. In a recent case, however, I have observed a potassium and non-protein nitrogen retention after the onset of diuresis. In this case the urine continued to approximate to a glomerular filtrate for several days. On theoretical grounds it was believed that, in the presence of a satisfactory urinary output, the excess potassium and nitrogen would be cleared by giving cortisone. This was done, and a dramatic fall in the serum potassium and non-protein nitrogen was observed. If the urine volume had not been sufficient, however, it would have been dangerous to use cortisone.

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"Egg white is the most alkaline natural fluid known, having a *p*H of about 9.5; this high alkalinity confers on it a definite bactericidal character, which is enhanced by the presence of certain proteins, such as lysozyme, a known antibiotic. The *p*H of yolk is about 7, and the whole egg therefore should act as an electric cell or battery because of the difference in acidity between the yolk and the white. The yolk, having an excess of positive hydrogen ions over the white, as it is more acid, ought to be at a positive potential relative to the white and should correspond to the positive pole of a cell. This difference in electric potentials within an egg can be demonstrated directly with the aid of a sensitive galvanometer. . . . The potential difference between yolk and white varies considerably from egg to egg and with the age of the egg; it is about 1/10 of a millivolt."—From a lecture given by D. P. Riley, D.Phil., at the Royal Institution on November 7, 1952.

GASTRIC ILEUS DUE TO POTASSIUM DEPLETION AFTER GASTRO-ENTEROSTOMY

BY

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Failure of the stoma to work is an unpleasant and common sequel of gastro-enterostomy done for obstruction at the pylorus or in the duodenum. The clinical features are familiar to all abdominal surgeons.

I wish to suggest that this condition is a gastric neuromuscular paralysis or ileus due to potassium depletion and that it may be treated successfully by giving potassium. Potassium is essential in neuromuscular activity. Paralysis of skeletal muscle due to potassium lack, and its cure by giving potassium therapeutically, have been known for many years. That potassium depletion may cause intestinal ileus has been suggested by Randall *et al.* (1949), Darrow (1950), and Streeten and Ward-McQuaid (1952).

Most of the obstructive situations in which gastro-enterostomy is employed are likely to result in potassium depletion. The reasons are various: low intake; the vomiting or aspiration of potassium-containing gastric juice; the excess tissue breakdown of starvation, leading to freeing of intracellular potassium and its consequent excretion by the kidneys; the administration of sodium, displacing potassium from the cell, and its consequent excretion—all are important. Displacement of potassium out of the cell for any reason will result in its excretion in the urine, for, so it is generally believed, there is no renal defence of potassium. Glycogen formation following the administration of glucose will result in the withdrawal of potassium from the extracellular fluid, though not from the body, since in this case it enters liver and muscle cells. Furthermore, it seems that to correct hypochloraemia in such a patient may be difficult unless hypopotassaemia be first corrected; and, if the unwise attempt is made, the great quantities of sodium necessarily given with the chloride will further deplete potassium and cause oedema. In short, both the obstruction and the usual therapy are likely to deplete body potassium, and the depletion will become the greater as urine flow is restored. The subject is discussed exhaustively by Darrow (1950), and by Randall *et al.* (1949) and Hawkins *et al.* (1951).

Case Report

The patient had an obstruction of the second part of the duodenum due to a gall-bladder carcinoma. On admission she was dehydrated, hypotensive, uraemic, hypochloraemic, alkalotic, and in tetany. At this stage the serum potassium was low, there was general weakness, and she had bradycardia and frequent extrasystoles. Hawkins *et al.* noted frequent extrasystoles in a similar situation. The data are shown in the Table.

After rehydration, restoration of serum chlorides, and restoration of urine flow a gastro-enterostomy was done on the seventh hospital day. There was not the expected flow of gastric contents into the jejunum. Aspiration volumes continued greater than oral intake. Parenteral water, sodium, and chloride were continued in order to restore blood pressure and chlorides from their post-operative fall. At this stage the serum potassium fell to 10.9 mg. per 100 ml., the tendon jerks disappeared, the patient was oedematous, and the stoma still was not working on the fifth post-operative day. Potassium administration up to this time had been in such cautious quantities as to be ineffective, and much of it was given orally. On this and the following day adequate potassium was given rectally and, in addition, on the evening of the fifth post-operative day 1.5 g. of potassium chloride was injected intravenously. Within a few hours gastric aspiration decreased to nil and oral nutrition was thenceforth satisfactory. Sudden let-through into the jejunum, occurring spontaneously, is the usual end of this syndrome. It is suggested that the gastric paresis was cured in this case before it would otherwise have happened and that it could have been prevented by early adequate parenteral potassium. Confirmation must obviously await further experience of the method.

The Materia Medica and Therapeutics of Potassium

For oral and rectal use iso-osmotic potassium chloride solution (1.15%) is suitable. For intravenous administra-

Hospital Day	Remarks	Water Intake (oz.)			Water Output (oz.)		Water Balance (oz.)	NaCl			KCl		Blood Urea (mg./100 ml.)	Blood Pressure
		Oral	I.V.	Rectal	Asp./Vomit	P.U.		Given (g.)	Serum Na (mg./100 ml.)	Serum Cl as NaCl (mg./100 ml.)	Given (g.)	Serum K (mg./100 ml.)		
1		19	0		12	0	+ 7	0						
2		27	100		2	8	+117	18						
3	Clinically alkalotic and uraemic; pulse 56; extrasystoles ++; jerks+	35	100		112	20	+3	27					328	130/60
4	Hands stiff	84	90		106	18+	+50	36	332	430	4·14	11·4		
5		71	100		112	52	+7	9	372	638	10·35	12·5 13·2		
6	Pulse 82, regular, good volume; remained so thereafter	101	50		110	59	−18	4·5	378	633	5·86		296	160/90
7	Gastro-enterostomy ..	95	100		116	29	+50	9						
8		7	80		118	31	−62	4·5						130/60
9	Incontinent; urine collection incomplete thereafter	3+	140		83	6+	< +54	18			4·14			
10	Oedema generalized ..	36	140		69	16+	< +91	13·5				15·1		160/90
11	Jerks absent	64	100		69	21+	< +74	18		500	2·76	10·9	184	
12	1·5 g. KCl intravenously in evening ..	57	40	20	62	19+	< +36	9	328	600	7·00	10·4		
13	Stoma working ..	67		80	12	4+++	< +131				9·86			
14		76		20		9+++	< +87				2·46			
15		102				28+++	< +74		329	575		14·5		
16	Jerks returning; haemoglobin 70% ..	75				22+++	< +53				3·79			
17	Oedema going ..													
18														160/90

tion quarter-strength iso-osmotic solution (0.28%) is suitable. The solutions are easily sterilized in the autoclave. For subcutaneous use Hawkins *et al.* recommend iso-osmotic solution with hyalase to facilitate absorption. Given subcutaneously, potassium chloride solution is painful, but with the usual clouding of consciousness these patients will not, at least initially, object. Given intravenously, potassium chloride rapidly produces a painful phlebitis. The vein usually remains patent, and such a phlebitis is not an indication for changing to another vein or stopping the infusion.

It is probably safe to give a potassium-depleted patient a pint (570 ml.) of quarter-strength iso-osmotic potassium chloride solution intravenously in two hours. It is also probably safe to give a pint (570 ml.) of iso-osmotic potassium chloride solution subcutaneously to a similar patient in four hours. Rapid estimations of serum potassium are necessary such as may be obtained with a flame photometer, and it is essential to check the serum levels daily or more often. In such a case as is here described potassium therapy should be started early and not when a pre-existing deficiency has been made worse by sodium and water administration. Nevertheless, potassium must not be given till rehydration is under way and a flow of urine has begun; otherwise fatal high levels may be attained in the extracellular fluid. Very great caution is required if there is associated renal disease or adrenal insufficiency. Potassium should not be given in the first 24 hours after operation.

I am indebted to Mr. Ian Fraser, in whose care this patient was, and to Sister Harrison, of the Musgrave Clinic, Belfast, for accurate records of treatment and for the devoted nursing which sustained this patient through a long illness.

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PAROXYSMAL PARALYTIC MYOGLOBINURIA

BY

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Paroxysmal paralytic myoglobinuria is a rare disease of unknown aetiology, affecting skeletal muscle and resulting in the liberation of myoglobin, which is excreted in the urine. The patient complains of painful muscle spasms and passes brownish urine.

Case Report

On December 13, 1946, a single woman aged 41 fell down "after a few gins" and sustained minor injuries. These were treated and she was sent home and advised to stay in bed. Three days later she suddenly developed cramps in both legs. At first the cramps were painless, but they soon became very painful and so severe that an hour later she was unable to stand. The pain started in the toes and spread upwards, first to the calves and then to the inner sides of the thighs.

On admission to hospital nothing relevant was found in her past medical or family history, and the temperature and pulse were normal. Physical signs were confined to the lower limbs, which were held extended with the feet in talipes equinus. All movements of the ankle-joints were limited by severe pain in the calf muscles, which were swollen, tender, and hard. Their "woody" consistency was similar to that felt in ischaemic contracture. The muscles on the medial side of the thighs were also tender, but their consistency was normal. All the signs and symptoms were more severe on the right side. The texture and colour of the skin were normal. The knee-jerks were normal, but the ankle-jerks were absent. The plantar reflexes were flexor, and there were no sensory changes. No pulsation could be felt in the popliteal, dorsalis pedis, and posterior tibial arteries on either side. Examination of the blood showed: red cells, 4,800,000; Hb, 96% (Haldane); white cells, 9,100 (polymorphs 80%, lymphocytes 15%, monocytes 4%, eosinophils 1%); platelets, normal; bleeding-time (Duke's) 2½ minutes; clotting-time 2¾ minutes; prothrombin time 15 seconds. Wassermann reaction and Kahn tests were negative and the Donath–Landsteiner reaction was also negative.

Diagnosis was difficult. Thrombosis of the deep veins of the calves was considered most likely, and, in view of the absence of arterial pulsation and the possibility of permanent ischaemic changes occurring in the muscles, it was decided to perform a decompressing operation on the worst side. On December 16 a vertical incision 8 in. (20 cm.) long was made through the skin and deep fascia of the right calf. Contrary to expectation, the calf muscles did not bulge, and they looked paler than normal. The wound was left open, dressed with penicillin powder and petroleum jelly gauze, and supported on a back splint. Intravenous heparin treatment was started, and intramuscular penicillin was administered. Next day the legs were less painful, though the calves were still hard and tender. The patient said that the right calf felt a little easier after the operation. On this day it was first noticed that the urine was dark red. Clinically the specimen suggested severe haematuria, but microscopical examination revealed only an occasional leucocyte, a trace of albumin, and a heavy deposit of phosphates. There were no red cells or casts.

It was the investigation of this apparent paradox of haematuria without red cells which led to the diagnosis. The next day the urine was still red, but the following day it was normal in colour. During the ensuing days the symptoms and signs slowly subsided, the calves becoming softer and less tender. On December 24, eight days after the decompressing operation, secondary suture of the wound in the right calf was undertaken, and a piece of the right gastrocnemius muscle was excised for examination. Healing by first intention followed. The serum potassium level while at rest in bed was 15.5 mg. per 100 ml., and a day later after a brisk walk it was 17 mg. She was discharged from hospital free from signs and symptoms three weeks after admission. Unfortunately it has since been impossible to trace the patient.

Spectroscopic examination of the urine on December 17 showed an alpha band at 585 mμ. On substituting oxyhaemoglobin for the urine there was a clear-cut shift of the band. The position of the absorption band suggested myoglobin (Theorell, 1934; Millikan, 1939). A crude preparation of myoglobin obtained from human muscle gave a similar band at 584 mμ. The pigment was tentatively identified as oxymyoglobin, and this finding was confirmed by Dr. J. C. White.

Professor Crawford reported on the muscle biopsy: "The specimen consists of skeletal muscle which shows a scattered lesion involving individual fibres, shrunken and separated from their sheaths; they stain poorly and the appearances suggest that myoglobin has diffused out from the fibres. There is some increase in the nuclei of the sarcolemma and of the interstitial fibrous tissue. Special staining shows patchy loss of striation in the affected fibres.

Serial sections have been examined, but they do not show any lesion of the blood vessels of the part. The appearances suggest a primary lesion of the muscle fibres, resulting in disintegration of the fibre, unassociated with vascular damage" (Figs. 1 and 2).

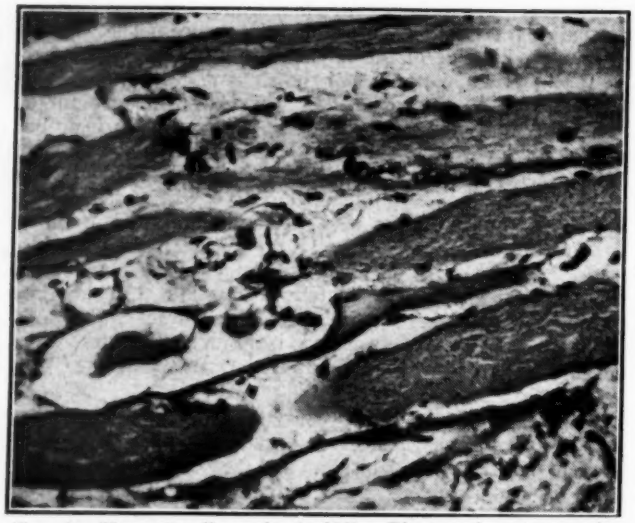

FIG. 1.—Haematoxylin-eosin (×200). Biopsy of gastrocnemius muscle showing localized necrosis of fibres surrounded by oedema and lymphocytic infiltration. One fibre is seen shrunken and separated from the sarcolemmal sheath.

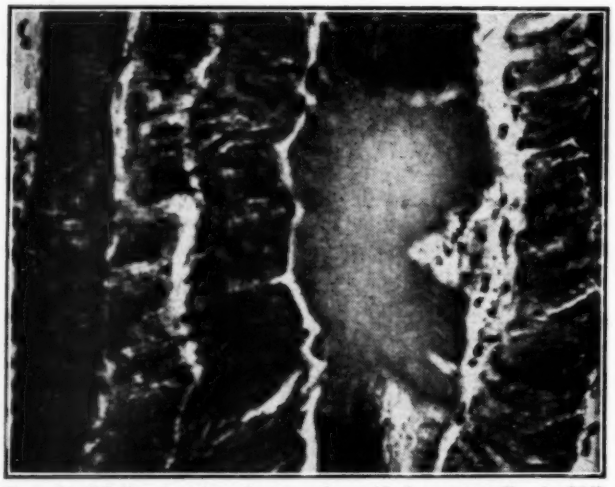

FIG. 2.—Mallory's phosphotungstic acid haematoxylin (×330). Same specimen as Fig. 1 showing strictly localized necrosis of muscle fibre with loss of striation and staining. The unaffected part of the fibre and the surrounding fibres show well-preserved striation.

The Literature

Up to the time of our observation, we could find only six case histories of this disease. Two further cases were ascribed to this syndrome (Millikan, 1939; Bywaters and Dible, 1943), but in one a clinical description was not available, and in the other the diagnosis was retrospective after death. Since 1946 five further cases have been described, three of them in the same family.

We owe the first description of the disease to Meyer-Betz (1910).

A 13-year-old boy was admitted to hospital in a state of collapse and apparently moribund. The disease started suddenly with abdominal pain, bleeding from the nose, and vomiting. He became very weak and a few hours after the onset voided some black urine. The family history revealed nothing. His past medical history showed that at the age of 10 his urine appeared to contain blood for two days, but he was not obviously ill. From that time he had "haematuria" once or twice a year, lasting for two days and associated with severe muscular weakness. About nine months before admission he had a more severe attack: he could hardly move and his urine was black. Four months before admission he had an attack of abdominal pain associated with severe weakness lasting for about 14 days. His mother noticed at this time that his legs and feet were swollen.

On examination the child could barely move. The lower extremities were more affected and were almost paralysed. The feet were in talipes equinus and the calf muscles contracted and hard. Passive movement of knee and hip caused pain. The elbows could not be straightened and there was limitation of wrist movement. The patellar reflexes were absent. All the muscles involved felt hard and tender to pressure. There was mild anaemia, with moderate leucocytosis.

The urine voided at the time of admission was chocolate-coloured and turbid, and showed a heavy deposit. There was some detritus, believed to be red cells, but no actual red cells were seen. A few granular and hyaline casts were also present. The test for albumin was strongly positive and spectroscopically the pigment resembled both oxyhaemoglobin and methaemoglobin. The output of urine was severely reduced during the first day, but its colour rapidly became paler and by the end of the second day the pigment had disappeared. At this stage hyaline, granular, and red-cell casts were seen in abundance. Gradually the urinary output rose and the child recovered. The contractures disappeared in this order: hands, flexors of left arm, flexors of right arm; last to disappear were the contractures of the most severely affected calf muscles. Within three months of the onset the child appeared to be normal again.

Two minor attacks involving only the calf muscles and leading to discoloration of the urine were also observed.

Meyer-Betz noticed the striking similarity between this condition and "paralytic equine haemoglobinuria," and, although unable to confirm the nature of the pigment, he was aware that myoglobin was involved.

The cases since observed closely resemble the first. The pattern is the same and the variation is only in the severity of the episodes. The Table summarizes the main features.

The onset is sudden. With minor attacks there is bilateral but not necessarily symmetrical involvement of the muscles of the lower limbs. The attacks, which are frequently repeated over a period of months or years, often follow exertion after a period of rest in bed. The calf muscles are most often affected; they are painful and feel wooden as if in tonic contracture. The feet are in the position of a ballet dancer, and the attack is followed within a few hours by transient myoglobinuria. The duration and intensity of myoglobinuria is proportional to the severity of the attack and to the extent to which the musculature is involved. It may well be that minor attacks are more common than hitherto believed, and are missed because the staining of the urine is not noticed. The attacks are not associated with neurological changes, either sensory or motor. There is no oedema or involvement of the overlying skin. The course is generally afebrile, except in severe attacks in small children. Normal red- and white-cell counts appear to be the rule, and the urine shows no red cells or stromata to account for the blood-stained appearance.

Major attacks differ only in extent. The involvement of muscles spreads upwards until all the skeletal muscles are affected; this leads to the apparent paralysis which is included in the name of the syndrome. Myoglobinuria is more intense and prolonged.

Even the most severe cases on record ended favourably; renal failure seems to be unusual. The attacks have a tendency to recur, but in several of the cases they became less frequent and ultimately disappeared. The remote prognosis is more difficult to assess. Case 1 was well—apart from some residual contracture of the calf muscles—a year later, when last seen. Case 2 had three lesser attacks in the next two years. We have been able to follow up Case 3 in France 16 years later, as her father is a medical practitioner. She had one severe and two milder attacks within three years of the onset, and then recovered completely. The other cases could not be traced.

Details of Cases in the Literature

Author	Case No.	Age	Sex	Family History	Course and Remarks
Meyer-Betz (1910)	1	13	M	None	History of several minor attacks. In hospital with very severe attack involving whole body. Later two minor attacks while under observation. Complete recovery a year later
Hittmair (1925)	2	41	F	,,	Onset with sudden major attack, starting in legs, ascending to trunk and arms. Recovery in 14 days. Second major attack a year later, followed by a lesser attack, and finally minor attack during following year. Recovery
Debré *et al.* (1934)	3	2½	F	,,	Major attack with generalized paresis. Febrile. Calves most affected. 10 months later identical attack. Milder attack a year later and a minor attack after a further 3 months. Complete recovery
Huber *et al.* (1938)	4	4	M	,,	Single attack of medium severity affecting lower limbs. Slight fever. Recovery
Louw and Nielsen (1944)	5	4	M	8 members of 5 generations affected by sex-linked recessive muscular disease starting in childhood. ?Progressive muscular dystrophy	History of repeated minor attacks involving calves only. Seen with minor attack at age of 10. Recovery. Myoglobin confirmed
Scherwin (1945)	6	38	M	None	Three attacks with atypical distribution and course. Oedema and red skin over muscles involved. ?Polymyositis. Outcome not known
Elek and Anderson (present case) (1946)	7	41	F	,,	Single minor attack. Myoglobin confirmed. Recovery
Hed (1947) ..	8	20	M	3 males of 6 siblings affected; 2 males healthy. No other family history of muscular disease. Mother diabetic	Several minor and some major attacks from age of 15. Attacks related to exertion on fasting. One mild attack observed. Abnormal sugar tolerance curve. Myoglobin in urine confirmed
,, ,, ..	9	19	M	Brother of Cases 8 and 10	History of minor attacks from age of 16. Related to exertion while fasting. Abnormal sugar tolerance curve. Carbohydrate-free diet for 24 hours was followed by severe attack. Myoglobin confirmed
,, ,, ..	10	18	M	Brother of Cases 8 and 9	History of minor attacks consisting of pain in legs and dark urine. Related to exertion
Wissler (1948)	11	6	M	3 brothers suffered from a form of muscular atrophy. 2 died	Single attack of medium severity observed. Slight fever. Myoglobin confirmed
Kreutzer *et al.* (1948)	12	39	M	None	History of repeated fleeting attacks. 3 attacks of medium severity observed. Attacks could be brought on by stretching of muscles. Myoglobin confirmed. Recovery, but no follow-up available

Differential Diagnosis

The relative ease with which myoglobin can now be identified spectroscopically sets myoglobinuria apart from any form of haemoglobinuria. Although all of them are uncommon, there are several conditions known in which this pigment or its decomposition products appear in the urine. In all these the primary lesion is in skeletal muscle. If there is a sufficiently severe lesion of muscle and enough circulation for absorption to occur myoglobinuria will ensue. Myoglobin is readily excreted by the kidneys (Camus and Paginez, 1902); its threshold is stated to be about 20 mg. per 100 ml. Above this value its excretion in dogs is proportional to the concentration in the blood (Yuile and Clark, 1941), which means that myoglobin is cleared about 25 times more rapidly than haemoglobin. The least amount to produce visible discoloration of the urine is about 40 mg. per 100 ml. This rapid excretion explains why in all but the most severe and widespread lesions of muscle the staining of the urine is very transient.

The conditions in which myoglobinuria is one of the cardinal signs may be summarized as follows (modified from Biörk, 1949): (1) Paroxysmal paralytic myoglobinuria; Haff disease. (2) Dermatomyositis with myoglobinuria; myositis following carbon monoxide poisoning; myoporphyrinuria. (3) Progressive muscular dystrophy. (4) Traumatic myoglobinuria: (*a*) "crush syndrome"; (*b*) electrical high-voltage accidents; (*c*) arterial occlusion with ischaemia.

Haff disease is undoubtedly the commonest cause of myoglobinuria in man. It occurs in East Prussia (Starfinger, 1924; Ewig, 1924; Meyer, 1924), Sweden (Berlin, 1944), and Karelia (Basharina and Kyrochkina, 1949). Its clinical features closely resemble the condition described by Meyer-Betz, and the histological findings, described by Kaiserling (1932), consist of focal lesions of individual muscle fibres. The pigment in the urine has been identified as myoglobin (Assmann *et al.*, 1933; Jeddeloh, 1939).

Dermatomyositis may also be associated with myoglobinuria, as in the case described by Günther (1924) and possibly also in Paul's (1924) case. In both the disease was characterized by rigors and high fever, and the severity of the muscular lesions was greater in the upper than in the lower extremities. Both terminated fatally. It may be that Scherwin's (1945) case should also be ascribed to this group, since there was oedema of the skin over the affected muscles. Myoglobinuria was not confirmed in any of these three cases, and the clinical picture was unlike that of paroxysmal paralytic myoglobinuria.

Carbon monoxide poisoning causes a severe form of myositis, sometimes with myoglobin in the urine (Günther, 1921, 1940; Brass, 1944).

Myoporphyrinuria is less well established as a disease entity; cases associated with muscle atrophy and loss of myoglobin have been described (Vanotti, 1935–6; De Langen, 1943; Belloni, 1947). Similarly the relationship of progressive muscular dystrophy to paralytic paroxysmal myoglobinuria is at present undefined. The resemblance of the distribution of the lesions was noticed early (Meyer-Betz, 1910; Kreutzer *et al.*, 1948). Louw and Nielsen (1944) found evidence suggestive of progressive muscular dystrophy in the family of their case and a similar family history in another case (Wissler, 1948). Furthermore, some authors are of the opinion that the primary injury in progressive muscular dystrophy is in myoglobin metabolism (Meldolesi, 1937, Meldolesi *et al.*, 1939).

The only group of known aetiology is that of traumatic myoglobinuria. Originally observed in the first world war (Frankenthal, 1916), it was studied by Minami (1923) and Husfeldt and Bjering (1937) and later most extensively by Bywaters and his associates (Bywaters, and Delory, 1941; Bywaters and Beall, 1941; Bywaters, Delory *et al.*, 1941; Bywaters and Popjak, 1942; Bywaters, 1944; Bywaters and Stead, 1944). Severe crush injuries or physical punishment (Langen, 1946) may cause necrosis of muscle, which, if severe enough, terminates fatally through renal failure. High-voltage currents similarly cause damage to skeletal muscle, often to a greater extent than the external injuries would suggest. Myoglobinuria and renal failure have been observed (Fischer and Rossier, 1947; Fischer and Fröhlicher, 1947). Ischaemic necrosis due to arterial thrombosis, embolism, or even spasm may simulate the conditions of traumatic myoglobinuria (Bywaters and Stead, 1945).

Aetiology

Little is known about agents causing acute necrosis of muscle. Myoglobinuria is, however, a common condition in animals (Minett, 1935). One form affecting horses is known as "paralytic myoglobinuria" (Fröhner, 1884; Camus and Pagniez, 1902, 1904; Camus, 1903), and the pigment has been identified (Carlström, 1931). The large muscles of the hind part are most severely affected and the onset is sudden. In "enzootic myoglobinuria" of horses (Wirth, 1921; Hobmaier, 1926; Stang and Wirth, 1928; Deubel, 1932; Bédaride, 1933) the muscles of mastication are affected. There is stiffness and swelling but no paralysis. Draught oxen and young calves suffer from "white muscle disease" (Vawter and Records, 1947), while lambs and young pigs suffer from a form of acute muscular necrosis, but the pigment has not been found in the urine (Hobmaier, 1926).

Foxes suffer from a disease known as Chastek paralysis, while in districts afflicted with Haff disease cats and even birds may suffer from it. The so-called "intermittent paralysis" of horses is said to be due to thromboses in the abdominal aorta (Carlström, 1931).

While the chain of events starting with acute muscular necrosis and leading to myoglobinaemia and myoglobinuria can easily be traced in all these conditions, and in recent years much has been learned about the renal lesions accompanying this sequence, practically nothing is known about the aetiology of acute focal muscular necrosis. In equine paralytic myoglobinuria excessive lactic acid formation was blamed, and this suggestion is reflected by Hed's statement that in his cases abnormal carbohydrate metabolism was responsible. Since the mother suffered from diabetes, the association may well have been accidental. Furthermore, there is no evidence of faulty carbohydrate metabolism in any of the other cases (Kreutzer *et al.*, 1948). Millikan's observation regarding excessive blood potassium levels is likely to be the result rather than the cause. Nor is there convincing evidence that human paroxysmal paralytic myoglobinuria is a hereditary condition. Its course and the long-term good prognosis make it unlikely, but this point cannot be settled until more information is available.

The condition resembles Haff disease in its clinical course, the low incidence of uraemia, and the histological changes found in the muscles, and may be a sporadic form of it. Haff disease is epidemic and so far all the outbreaks have stopped before it could be decided whether a virus or a toxic agent was responsible. Eating tainted fish is believed by many to be the cause. In this respect it may be noteworthy that Chastek paralysis of silver foxes, in which there is severe damage to muscles, is due to feeding on certain raw fish. The symptoms of this disease can be produced experimentally by a diet deficient in vitamin B_1, and recovery follows administration of this vitamin. A substance, probably a protein, has been recovered from fish that inactivates vitamin B_1 (Ågren, 1944). So far intravenous aneurin has not been tried either in Haff disease or in paroxysmal paralytic myoglobinuria, but on the basis of this theory it should bring about rapid recovery. Apart from our case, there is no information available about the lesions in the muscle as they appear in the acute phase, since no biopsy has been taken in any of the other cases. In one of Hed's cases a biopsy between attacks showed no abnormality except for a little diffuse increase of fibrous tissue between the muscle fibres. This suggests that, whatever the aetiological agent, the paroxysms of myoglobinuria represent the onset of necrosis in the muscles, possibly aggravated by exertion.

Summary

Paroxysmal paralytic myoglobinuria is briefly reviewed and a case illustrating the syndrome described.

The disease occurs in minor and major forms, which differ only in the extent of the lesions. Minor forms are characterized by painful tonic spasms affecting the lower limbs, mainly the calf muscles, followed within a few hours by transient myoglobinuria. This pigment is suggested by the colour and by the absence of red cells or stromata. Major attacks consist of pseudoparalysis of the whole body, and are rarer. The disease has a tendency to recur, but the prognosis is good. The pathological changes in the affected muscles consist of focal necrosis. The aetiology is unknown.

We thank Sir Claude Frankau for permission to publish this case; Professor Theo. Crawford for his pathological investigations and for the use of the photomicrographs; and Dr. J. C. White and Mr. T. Pringle for the biochemical investigations.

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In the second number of *Scientific Film Review* there are assessments of four medical films: "Dextran—The New Narrow Fraction" (Benger Laboratories Ltd.), "The Effect of Metallic Ions and Osmotic Disturbances on the Heart" (U.S. Information Service: Indiana University), "Gastric Secretion" (Imperial Chemical Industries), "The Mitral Valve" (Montefiore Hospital, New York), and "Senile Obliterative Arteritis of the Legs" (Ciba Laboratories Ltd.). There are also reviews of three films on human reproduction, intended for schoolchildren and others. *Scientific Film Review* is obtainable from the British Film Institute, 164, Shaftesbury Avenue, London, W.C.2. Annual subscription 5s., single copies 1s. 6d.

SPLENECTOMY IN THREE CASES OF MYELOPHTHISIC ANAEMIA

BY

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Myelophthisic anaemia, a comprehensive term denoting anaemia associated with reduced cell formation by the bone marrow and compensatory haemopoiesis in other organs, is generally accepted as the one absolute contra-indication to splenectomy. The spleen is regarded as the main focus of the extramedullary haemopoiesis, and therefore essential for the maintenance of the patient's life.

This paper describes three patients with myelophthisic anaemia in whom splenectomy was performed. One of them benefited greatly from the operation, one temporarily, whilst the third, although not improved, did not appear to be materially harmed. It is suggested that the improvement caused by the splenectomy was due to the removal of an important haemolytic component of the anaemia.

Case 1

A white man aged 31 complained of having felt tired at the end of the day's work for a few weeks before coming to hospital in February, 1950. Food "felt too hard for his stomach," and on several occasions he vomited immediately after a meal. There was no blood in the vomit. His appetite diminished, but he noticed no loss of weight. During the five days before admission he felt increasingly weak and had three attacks of shivering and sweating. Since the age of 16 he had suffered from occasional epistaxes. About a year before admission these nose-bleedings occurred every morning for a period of a few months. In 1944 he contracted malaria while in the Navy, and he had what was possibly a second attack in 1946, and a recurrence three months before admission. In 1947 he was examined for life assurance and was told that his spleen was enlarged. Since then he had been aware of a lump in his abdomen, but had no pain in that region and noticed no alteration in the size of the lump. There was no relevant family history.

On examination the patient was seen to be well nourished, with a sallow slate-brown pigmentation of the skin. Small lymph nodes were found in the cervical, axillary, and epitrochlear regions. The spleen, firm but not tender, extended into the left iliac fossa and 2.5 cm. across the midline. The firm edge of the liver was felt 3 cm. below the costal margin. While in hospital he had an irregular fever occasionally reaching 102° F. (38.9° C.). No malaria parasites or leishmania protozoa were found in blood and bone-marrow smears. Wassermann and Berger blood reactions, blood cultures, and *Brucella* agglutination tests were all negative. Serum proteins and liver-function tests were normal, and there was no excess of bilirubin in the serum. Radiographs of the whole skeleton were normal.

On admission the blood findings were: P.C.V., 22%; haemoglobin, 7 g. per 100 ml.; leucocytes, 3,500 per c.mm. (neutrophils 62%, eosinophils 2%, lymphocytes 28%, monocytes 8%); platelets, 63,000 per c.mm.; reticulocytes, 2%. The blood smear showed marked anisocytosis and poikilocytosis. In the first smear no immature cells were found, but after a few days 2 normoblasts per 100 leucocytes were counted and a similar number were regularly seen afterwards.

Eight sternal and iliac crest punctures failed to produce bone marrow. A sternal trephine biopsy was therefore performed, and the histological examination of the material obtained showed some fibrous tissue and some cells resembling histiocytes, but no haemopoietic tissue.

Course and Treatment.—On February 22 the patient had a severe epistaxis which reduced the volume of packed red cells to 18%. He was given 3 pints (1.7 litres) of blood, and the next day the volume was 28%. One month later the volume had dropped to 22%. On March 30 he was given 4 pints (2.3 litres) of blood and left hospital. He was readmitted on May 18, when his packed cell volume had dropped to 15%. He was again given 4 pints (2.3 litres) of blood, which raised the volume to 35%. Subsequently he was treated outside hospital, where his condition steadily deteriorated. From information obtained it appears that he received 18 pints (10.2 litres) of blood during the next three months. On August 21 splenectomy was performed by Mr. M. Cole-Rous, acting in consultation with Dr. B. G. Shapiro. The spleen weighed 3,300 g., and histological examination showed the changes of Gaucher's disease, increased haemosiderin in the swollen histiocytes, and myeloid metaplasia. After the operation the patient's condition improved rapidly. He returned to work in October, 1950, and has since, without treatment of any kind, felt perfectly fit.

On October 20, 1952, more than two years after the splenectomy, a blood examination showed: P.C.V. 49%; haemoglobin, 16.2 g. per 100 ml.; leucocytes, 9,100 per c.mm. (myelocytes 4%, neutrophils 56%, eosinophils 2%, basophils 1%, lymphocytes 29%, monocytes 8%); platelets, 430,000 per c.mm.; reticulocytes, 6%. In the blood smear one erythroblast and three normoblasts per 100 leucocytes were counted.

Comment.—This patient presented with Gaucher's disease of unknown duration, a grossly enlarged spleen, a slightly enlarged liver, and a haematological picture of myelophthisic anaemia. In spite of numerous blood transfusions his condition deteriorated rapidly, but after splenectomy a dramatic improvement took place. More than two years after the operation he lives a normal life and his blood picture is virtually normal, although the leuco-erythroblastosis might be interpreted as evidence of persistent extramedullary haemopoiesis.

Case 2

A white man aged 66 was admitted on February 25, 1952, with a typical history of gout of eight years' duration: repeated attacks of excruciating pain and swelling of the metatarso-phalangeal joint of his left big toe, with occasional involvement of his left ankle and at one stage his left elbow. Undue strain, exercise, or alcohol might bring on the attacks, which responded promptly to the administration of colchicine. Within three weeks of the onset of the gout he began to feel tired and out of sorts and easily became short of breath. His doctor found "a large spleen and anaemia," and his blood count at the time was: red cells, 4,300,000 per c.mm.; haemoglobin, 12.2 g. per 100 ml.; white cells, 6,920 per c.mm. (neutrophils 65%, eosinophils 4%, basophils 1%, lymphocytes 27%, monocytes 3%). The peripheral blood smear showed anisocytosis, poikilocytosis, and an occasional normoblast. The platelets appeared to be normal. He was given iron by mouth, liver injections, and *x*-ray therapy to the splenic area, and, although the treatment did not materially alter his blood picture, he felt well during the following years, apart from his attacks of gout. Two months before admission he became increasingly short of breath. After an attack of whooping-cough the dyspnoea was even more noticeable, and this was his only symptom. There was no history of gout or other relevant diseases in his family.

On examination the patient was obviously pale. His joints appeared normal except for an enlarged olecranon bursa at the right elbow. No enlarged lymph nodes were felt. His blood pressure was 125/55 mm. Hg. The spleen was firm, smooth, not tender, and was enlarged to 13 cm. below the

costal margin. The liver was felt 5 cm. below the rib margin and appeared to be of normal consistence. Special investigations showed : Urine, normal ; blood urea, 68, 47, and 28 mg. per 100 ml. on different occasions ; serum uric acid, 7.8 mg. per 100 ml. ; serum creatinine, 2.76 mg. per 100 ml. ; serum albumin, 4.7 g. per 100 ml. ; serum globulin, 3.1 g. per 100 ml. ; serum van den Bergh, direct and indirect negative ; thymol turbidity, 1 ; thymol flocculation, 1 ; colloidal gold, 0. Radiographs of the pelvis, femora, and skull were normal.

Blood examination showed : P.C.V., 25% ; haemoglobin, 8.5 g. per 100 ml. ; leucocytes, 2,500 per c.mm. (neutrophils 55%, lymphocytes 45%) ; platelets very scanty ; reticulocytes, 2%. The peripheral blood smear showed anisocytosis. poikilocytosis, and occasional myelocytes and normoblasts.

Five attempts to obtain bone marrow by needle biopsy failed. Trephining of the sternum was done, and, surprisingly, the marrow was found to be extremely cellular and

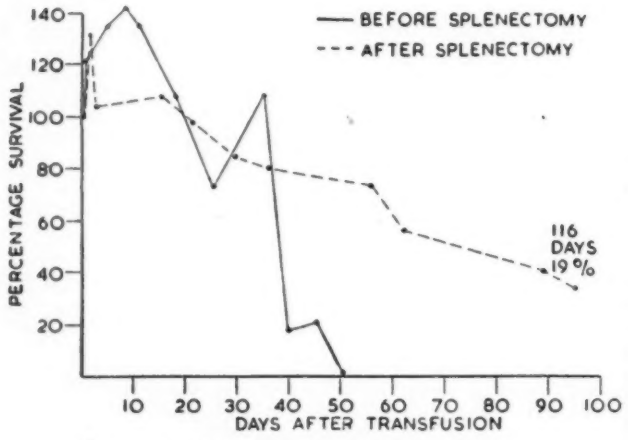

FIG. 1.—Red-cell survival curves of Case 2.

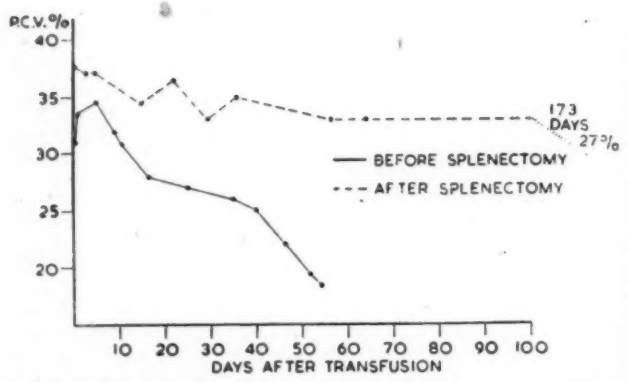

FIG. 2.—The packed cell volumes of Case 2 before and after splenectomy.

of normal composition. The differential count of the marrow gave this result : Myeloblasts, 0.66% ; promyelocytes, 1.33% ; myelocytes, 4.66% ; metamyelocytes, 7.33% ; eosinophil myelocytes, 0.66% ; neutrophils, 33.33% ; eosinophils, 1% ; lymphocytes, 8.33% ; monocytes, 1% ; early erythroblasts, 2% ; late erythroblasts, 13.66% ; normoblasts, 26%. The report on the histology of bone-marrow sections read : "Histologically there is definite evidence of myelosclerosis. The trabeculae are thickened with prominent cement lines, and, whilst osteoblastic activity is on the whole slight, woven bone is being formed in some areas. Myelofibrosis, on the other hand, is absent, there being occasional foci only of plump fibroblasts. The bone marrow is very cellular, with numerous blasts and more mature cells of both red and white cell series. Megakaryocytes appear to be in excess."

Red-cell survival was estimated by the Ashby technique (Dacie and Mollison, 1943), and was found to be shortened (Fig. 1).

Course and Treatment.—Ferrous sulphate, 18 gr. (1.2 g.) daily, was given for two months without improvement of the patient's anaemia. He was given a transfusion of 4 pints (2.3 litres) of blood, which resulted only in a brief improvement (Fig. 2). After the transfusion his gout became worse and the dosage of colchicine had to be increased to control his acute symptoms. After further transfusion splenectomy was performed on May 2, 1952, by Mr. E. Malherbe. A small spleniculus, a lymph node at the hilum of the spleen, and a small piece of liver were also removed. The spleen weighed 1,600 g., and histological examination revealed pronounced myeloid metaplasia with gross excess of megakaryocytes. Evidence of blood destruction was shown by changes in the cells lining the splenic sinuses and the presence of altered pigment. A differential count on smears made from splenic pulp gave this result : Myelocytes, 6.33% ; metamyelocytes, 6% ; neutrophils, 12.66% ; lymphocytes, 70% ; monocytes, 1% ; normoblasts, 4%. Numerous megakaryocytes were seen. The lymph node showed evidence of blood destruction by the presence of altered blood pigment and active macrophages, but haemopoiesis was trifling. The sinusoids of the liver contained a large number of megakaryocytes, but there was no indication of haemopoiesis.

The patient's gout flared up after the operation, but was controlled by three days' treatment with A.C.T.H. followed by colchicine. The survival rate of transfused red cells was now normal (Fig. 1) ; the improvement is also reflected in the almost steady packed cell volume without further transfusions (Fig. 2). The patient has felt well, and has been practically free of the symptoms of gout. A blood examination on October 21, nearly six months after splenectomy, showed : P.C.V., 27% ; haemoglobin, 9.5 g. per 100 ml. ; leucocytes, 38,000 per c.mm. (myelocytes 2%, metamyelocytes 7%, neutrophils 74%, basophils 1%, lymphocytes 16%) ; platelets, very numerous ; 9 normoblasts per 100 leucocytes were counted.

Comment.—This patient showed the classical picture of gout combined with the syndrome of myelophthisic anaemia. The hyperplastic bone marrow in this combination is apparently rather characteristic (Reifenstein, 1945 ; Merskey, 1949), but in this case there was definite myelosclerosis. There was a very close association between the onset of gout and the beginning of the symptoms due to anaemia ; furthermore, once the spleen was removed and the blood count stabilized the gout virtually ceased. It is likely that the gout was related to the intensity of the haemolytic process. The haemolytic element in the increasingly severe anaemia was clearly demonstrated by the short survival of transfused red cells, and the part played by the spleen in this phenomenon may be inferred by the return to normal of the red-cell survival time after splenectomy. This improvement was reflected in the clinical condition, and the patient lived a normal life. The remission was not complete and on October 23 he was readmitted for another blood transfusion of 6 pints (3.5 litres) of blood. Sixty-seven days after this transfusion he was again transfused with a similar volume of blood, but only 51 days elapsed before blood was again required. During the last transfusion period he was on continuous cortisone therapy (75 mg. a day after an initial loading dose).

Case 3

A white woman aged 58 was referred to hospital because of unexplained anaemia and splenomegaly. She had been given the usual haematinics without improvement and had been maintained only on blood transfusions. She had suffered from mild hypertension for years, and for the past four years had complained of general weakness. One year previously an obscure episode occurred during which she may have vomited a little blood. She thinks that her doctor did a venesection and removed a "a pint or two of blood." After that she was unable to walk for six months, and

then she slowly recovered a little. She could not recall losing blood in other ways. Her appetite had been poor for months.

On examination she was seen to be anaemic. Her heart was slightly enlarged and her blood pressure was 170/90 mm. Hg. There was no adenopathy. The spleen was firm and smooth, but not tender, and was enlarged to the level of the umbilicus. The liver was felt 5 cm. below the costal margin. Gall-stones were demonstrated by a cholecystogram, but the gall-bladder excreted the dye fairly well. Barium enema and two barium-meal examinations gave normal results.

Blood examination showed: P.C.V., 15%; haemoglobin, 6.4 g. per 100 ml.; leucocytes, 3,300 per c.mm. (myelocytes 1%, metamyelocytes 4%, neutrophils 33%, eosinophils 1%, basophils 1%, lymphocytes 58%, monocytes 2%); platelets, numerous; reticulocytes, 4%. The blood smear showed marked anisocytosis, poikilocytosis, and polychromasia. Two erythroblasts and seven normoblasts per 100 leucocytes were counted.

Marrow puncture was attempted in two areas of the sternum and in two sites on the left iliac crest. The fluid

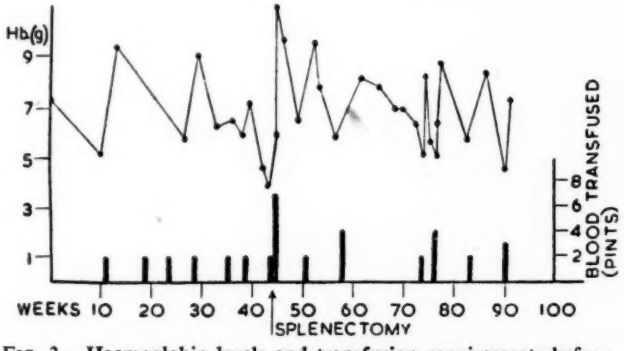

FIG. 3.—Haemoglobin levels and transfusion requirements before and after splenectomy in Case 3.

obtained appeared to be identical with the peripheral blood. Trephining of the sternum was done; smears made at the operation also appeared to be similar to the peripheral blood. Sections of the marrow showed the changes of myelosclerosis. The medullary cavity was traversed by thick bony lamellae and the scanty residual spaces contained some fibrous tissue, oedematous adipose tissue, a few osteoclasts, and an occasional lymphocyte and plasma cell. Myeloid cells were practically absent.

Course and Treatment.—The patient was kept under observation for some 40 weeks. Repeated blood transfusions were essential to keep her alive (Fig. 3). Splenectomy was therefore performed by Mr. J. Heselson. The spleen weighed 1,400 g., and the striking histological feature was active haemopoiesis, both myeloid and erythrocytic. Megakaryocytes were numerous. Erythrophagocytosis was slight, but there was an excess of haemosiderin pigment. The walls of the sinusoids were thickened, and within the sinusoids themselves haemopoiesis appeared to be proceeding. For a short time after the operation the patient felt a little better, but her blood-transfusion requirements remained unaltered (Fig. 3). Cortisone was tried in full dosage for six weeks without effect. The patient was still alive more than a year after the splenectomy, but her blood status had not improved.

Comment.—This was clearly a case of myelophthisic anaemia with myelosclerosis of unknown origin in which the patient could be kept alive only by repeated blood transfusions. Splenectomy did not improve the condition, but it did no harm.

Discussion

These three cases conform to the diagnosis of myelophthisic anaemia. The complete syndrome consists of a reduction of all the formed elements of the blood with some, usually few, immature red and white cells in the peripheral blood—the so-called leuco-erythroblastosis. Bone marrow is difficult or impossible to obtain by needle biopsy, and when trephining is done the marrow is often found to be fibrosed or sclerosed and the cellular composition is characteristically similar to that of the peripheral blood. Areas of hyperplastic marrow may be found. The spleen is grossly enlarged and there is slight hepatomegaly. Splenic puncture may assist in the diagnosis by demonstrating the myeloid metaplasia (Moeschlin, 1951). Radiography of the skeleton may show increased density of the bones.

The commonest cause of the syndrome is encroachment on the bone marrow by foreign cells as in carcinomatosis or the lipoidoses, as in Case 1. Poisoning of the bone marrow by chemicals such as benzene or carbon tetrachloride may give rise to the condition; and, finally, a group of cases is found in which the aetiology is obscure, and this group has therefore been given a confusing array of descriptive names: myelosclerosis, agnogenic myeloid metaplasia, aleukaemic megakaryocytic myelosis, etc. Case 3 apparently belongs to this ill-defined group.

If the conception of hypofunction of the bone marrow with compensatory extramedullary haemopoiesis is correct it would seem logical to believe that the removal of the main focus of this haemopoiesis, the spleen, would be deleterious to the patient. Splenectomy in myelophthisic anaemia has therefore persistently been condemned (Downey and Nordland, 1939; Carpenter and Flory, 1941; Bodley Scott, 1949; Wintrobe, 1951; Learmonth, 1951; Moeschlin, 1951; Chatterjea, Arrau, and Dameshek, 1952; Whitby, 1952). When the operation has been carried out the results have been poor, if not disastrous. Hickling (1937) reviewed 27 reported cases: in 15 the patient died a few days after the splenectomy, while those that survived the operation did not improve and most were dead within a year.

As an exception to this general rule a few cases of myelofibrosis and myelosclerosis have been described in which splenectomy was beneficial (Engell, 1947; Edwards, 1951; Franks, 1952; Andersen and Sørensen, 1952), and of the three cases reported above one showed great improvement, one temporary improvement, and one did not deteriorate.

From the evidence presented, especially the rapid elimination of transfused cells in Case 2, it would seem that in some instances of myelophthisic anaemia an important element of haemolysis plays a part in the pathogenesis, and that this red-cell destruction may outweigh the haemopoiesis in the spleen. Whether this haemolysis is a manifestation of "hypersplenism" is an academic point beyond the present discussion. The important fact is the demonstration that in some cases of myelophthisic anaemia the overwhelming haemolysis may be arrested by the removal of the spleen and the patient's condition thereby improved.

The problem must now be to decide which cases to choose for splenectomy. Morrison *et al.* (1951) would limit the operation to cases in which splenic myeloid metaplasia is absent, but this criterion seems too rigid. If the patient is losing ground in spite of repeated blood transfusions, and especially if it can be demonstrated that the red-cell elimination is exceedingly rapid, the question of splenectomy should seriously be considered.

Summary

Three cases of myelophthisic anaemia are described—one due to Gaucher's disease, one associated with gout, and a third of unknown aetiology. The first was greatly improved after splenectomy, the second was temporarily improved, and the third, while little better, did not deteriorate.

Splenectomy is generally contraindicated in myelophthisic anaemia, but it is suggested that with evidence of rapid cell destruction, possibly demonstrated by a short survival rate of transfused cells, it is worth while considering splenectomy as a last resource.

We have to acknowledge the assistance given to us by Professor F. Forman, in whose department this work was carried out. The red-cell-survival studies were done in conjunction with the C.S.I.R. research unit (Professor J. F. Brock). The cases were in the charge of the following clinicians, and we are indebted for their constant co-operation: Drs. M. Cole-Rous, J. Heselson, W. P. U. Jackson, A. Landau, E. Malherbe, M. Nellen. The histological examinations were kindly carried out by Professor J. G. Thomson, Dr. G. Selzer, and Dr. R. G. F. Parker. We were both in receipt of grants for research expenses from the Staff Research Fund, University of Capetown. The work was done with support from the Lady Tata Memorial Trust.

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VALUE OF PRIMIDONE IN EPILEPSY

BY

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Since the introduction of primidone ("mysoline"; 5-phenyl-5-ethylhexahydropyrimidine-4 : 6-dione) as an anticonvulsant drug some two years ago, two papers have appeared on its use in the treatment of epilepsy. A report of its initial trial at the David Lewis Epileptic Colony was given by Handley and Stewart (1952). Of the 40 patients treated all of whom had had prolonged treatment with other drugs, 12 had complete abolition of all types of attack over the six-months period of trial, and a further 11 showed a reduction of two-thirds or more. Butter (1953) recorded his results also from a special hospital for epileptics, where 58 patients had been treated. Again all had had extensive previous treatment. During 15 months only 3% had their fits abolished, but 50% derived some benefit. The results in both these reports must be regarded as very promising in view of the type of case treated. The present paper records our experience in the treatment of both symptomatic and idiopathic epileptics from the routine outpatient practice of a neurological clinic.

Case Material

Seventy patients of whom detailed records were available are considered here, though a further 12 have been treated; 43 were male and 27 female, and their ages ranged from 4½ to 60 years. Twelve had post-traumatic epilepsy—four from closed head injuries and eight from brain wounds; 10 had symptomatic epilepsy from proved brain lesions such as neoplasm or vascular accident; the remaining 48 cases were regarded as idiopathic. In Table I the cases are grouped according to the predominant type of fit or fits that they had. However, all those listed as having focal fits did have an occasional grand mal with the focal attack as an aura. The 31 patients in group 1 had mainly grand mal—10 with a definite aura; 8 (group 2) had both petit and grand mal; 4 (group 3) had psychomotor epilepsy; 10 (group 4) had psychomotor and grand-mal attacks; 10 (group 5) had petit mal only; 7 (group 6) had focal attacks—2 motor, 3 sensory, and 2 visceral.

TABLE I.—*Results of Primidone Treatment in Different Types of Epilepsy*

Group	Much Improved	Improved	No Change	Worse	Total	Treatment Abandoned
1. Grand mal only ..	11	14	2	2	29	2
2. Grand mal and petit mal ..	1	5	2	0	8	0
3. Psychomotor attacks ..	0	2	2	0	4	0
4. Grand mal and psychomotor	4	2	2	1	9	1
5. Petit mal only	2	2	3	1	8	2
6. Focal attacks	2	4	1	0	7	0
Total ..	20	29	12	4	65	5

Dosage.—This varied from 1.5 to 0.375 g. a day. At first a routine of three or four 0.25-g. tablets a day was used, but later an initial dosage of half a tablet thrice daily was adopted, as this produced less drowsiness. It was noted in some early cases that the substitution of primidone for phenobarbitone and sodium hydantoinate produced a modification of the attacks, but not always an actual reduction. As a result hydantoins were tried in conjunction with primidone, and the combination appeared to be more effective. In general, therefore, our initial dosage scheme has become primidone, 0.125 g. (2 gr.) and hydantoin, 0.05 g. (¾ gr.) each thrice daily, and this is adjusted in the light of clinical response. A combination of primidone and barbiturates, though occasionally used, has often proved unduly soporific. Primidone alone, however, has been used in 15 cases, with definite improvement in seven.

In five cases toxic symptoms caused the drug to be abandoned in from 10 days to two months of the start of treatment. Of the remaining 65, 12 were treated for less than six months, 23 for six to 12 months, 16 for 12 to 18 months, and 14 for 18 to 24 months. All had had previous treatment, usually for some years, with barbiturates, hydantoins, and sometimes troxidone; and it was because fits continued despite this that primidone was tried.

Results

The results of treatment in each of the six types of attack are shown in Table 1. Those whose attacks were abolished or so reduced as to be negligible so far as their ordinary activities were concerned were regarded as *much improved*; when attacks were reduced by 50% or more they were regarded as *improved*. Reduction was assessed by comparison with the frequency during the year previous to starting primidone. Only those whose actual attacks were increased were labelled "worse," other toxic effects of the drug being considered separately. It will be seen that the best results were obtained in the grand mal and grand mal and psychomotor groups. There are, however, aspects of the drug's action which do not emerge from these figures alone. In groups 1 and 4 there was sometimes a striking improvement in general social behaviour—irritability and perverseness being noticeably reduced. Relatives often remarked on this, and it is important in assessing the drug's value as a remedy in epilepsy rather than solely as an anticonvulsant. In three of the four cases of group 5 who showed improvement, this was unexpectedly delayed. In one, for instance, there had been no improvement after three months and treatment was to be abandoned at the next visit two months later. However, by then attacks were beginning to lessen, and nine months after the onset of treatment they had been completely abolished.

TABLE II.—*Results of Primidone Treatment in Traumatic, Symptomatic, and Idiopathic Epilepsies*

Type of Epilepsy	Much Improved	Improved	No Change	Worse	Total	Treatment Abandoned
Traumatic ..	4	7	0	0	11	1
Symptomatic ..	0	5	4	1	10	0
Idiopathic ..	16	17	8	3	44	4

In Table II the results are compared in the idiopathic, traumatic, and symptomatic cases. There is no significant difference between the traumatic and idiopathic. Of the symptomatic ones, five (two improved, two no change, one worse) had a presumed progressive organic cause) so that their poorer response was to be expected. These also weight the overall results in Table I.

In Table I cases are grouped on a clinical basis. However, since the electroencephalogram (E.E.G.) pattern appears to correlate more highly than the clinical description of the attack with response to the oxazolidinediones, results are given in relation to E.E.G. records in Table III for the

TABLE III.—*Clinical Results of Primidone Treatment in Relation to Varying Electroencephalogram Patterns*

E.E.G. Pattern	Much Improved	Improved	No Change	Worse	Total
3 cps. wave and spike ..	3	2	1	1	7
2 – 4 cps. bilateral paroxysm	2	1	1	0	4
Generalized dysrhythmia	2	2	1	0	5
Localized or focal spikes: atypical wave and spike	9	14	6	3	32
Bilateral theta paroxysm	4	9	3	0	16
Normal record	0	1	0	0	1
Total	20	29	12	4	65

65 patients who continued treatment. There does not seem to be any great difference in the clinical response of the varying E.E.G. patterns.

Those cases with localized or focal spike discharges and atypical wave and spike rhythms most often had these abnormalities in leads from the temporal regions. Clinically, also, they showed a high incidence of psychomotor attacks and the milder conduct disorders sometimes associated with epilepsy. In general, therefore, they represent what have recently tended to be described as "the temporal lobe epilepsies." The record of some improvement in 23 out of the 32 cases is therefore of special interest.

When alterations in seizures are considered in detail in a given case an interesting point emerges. In grand mal attacks with an aura, the grand-mal element may be controlled while the aura continues or even becomes aggravated. In one patient a series of brief sensory attacks in one arm usually lead up to a grand-mal convulsion. For the first few weeks of treatment the sensory attacks became prolonged, so that for some 12 hours a continuous sensation occurred, similar to the previous attacks, but no grand mal developed and the sensation slowly cleared. Addition of hydantoin curtailed this aura, and some months later there were no grand-mal attacks and only occasional brief sensory attacks. A similar effect was noted in three other patients. In one the prolongation of an abnormal sensation was so unpleasant that she refused to continue the drug.

Toxic Effects

In general primidone seems singularly free from toxic effects, and when they occur they are usually mild and transient.

Routine blood counts and urine tests were done in the first 15 patients, but as they showed no abnormality they were abandoned for subsequent cases. Thirty-six patients complained spontaneously of drowsiness at the start of treatment. A further 22 mentioned this in reply to questions. It usually cleared in a week or two, but 12 patients were still troubled by it months later. A few also described mild confusion and inability to concentrate. In three this was so marked as to constitute a mild confusional psychosis, and in all three of them paranoid trends appeared. In two the drug was abandoned because of this and in the third it was restarted in a smaller dose, with benefit. Two patients had an urticarial rash soon after starting the drug; blood counts were normal and the rash did not reappear when the drug was begun again after an interval. Transient nausea, giddiness, and ataxia occurred in four cases, and, in one, treatment had to be given up. In two vomiting was troublesome: one refused to continue the drug because of this, the other continued with a smaller dose after an interval, with no return of sickness.

Two patients who omitted the drug abruptly and without medical advice developed marked increase in their grand-mal attacks—in one amounting to a mild status epilepticus. It seems best to curtail primidone gradually if possible. In this respect it may be similar to the barbiturates and hydantoins, and unlike troxidone, which does not carry this risk of provoking status epilepticus if stopped suddenly.

Apart from the five cases in which treatment was given up early for the reasons mentioned above, in four it was omitted after three to six months because the fits seemed to be worse; and in a further ten, after a trial of six to nine months, as there was no improvement.

Conclusions

Primidone seems to be of some value in all types of epilepsy. However, the impression is gained that it is less useful in petit mal than in grand mal, while the proportion of psychomotor cases which are improved is especially gratifying, since this type is usually resistant to other anticonvulsants. It may be that it will find a special application here; though more prolonged experience is required, because temporary improvement from any change of drug has so often been misleading in the past.

Apart from its anticonvulsant action, it seems to benefit the milder behaviour disorders, those angularities of conduct from which some epileptics seem to suffer. The relatively high incidence of these in the "temporal lobe epilepsies" suggests that neuronal circuits in this region may be especially implicated and that the drug may act specifically on these. Its evident though mild soporific effect, since this is shared with other anticonvulsants, cannot wholly account for the benefit.

The results reported here are the more striking because this series is a highly selected one, most cases having failed to respond adequately to all the usual anticonvulsants. However, the absence of any serious toxic effects suggests that primidone should be given adequate trial as the drug of first choice in the routine treatment of epileptics.

Summary

Results of primidone treatment in 70 cases of epilepsy whose response to other anticonvulsants had been unsatisfactory are given—48 were idiopathic, 12 traumatic, and 10 symptomatic. Thirty-one had grand mal, eight mixed grand and petit mal, 10 petit mal only, 14 psychomotor attacks with or without grand mal, and seven focal attacks. Forty-nine cases showed improvement, and this occurred in all types of attack. In view of the usually poor response of psychomotor attacks to anticonvulsants, some improvement in eight out of 13 patients who continued treatment is of special interest. Toxic effects are usually mild and transient. In five cases they caused early cessation of treatment, in two probably unnecessarily.

Thanks are due to Imperial Chemical Industries Ltd. for early supplies of the drug for clinical trial; and to Miss F. M. Taylor and Miss F. Boselli for taking the E.E.G. records.

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PARAPLEGIA DUE TO PAGET'S DISEASE (OSTEITIS DEFORMANS)

BY

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Osteitis deformans, or Paget's disease, may affect any part of the skeleton in those of older years. While involvement of the spinal column is frequent, it is unusual for compression of the spinal cord to be produced. It is probable that this complication is commoner than the literature would indicate, as it occurs in an age group in which accurate assessments of the nervous system are rarely made. Two cases are described and their relationship to the usual pattern of the disease discussed.

Case 1

A woman aged 64 was admitted to Dunedin Hospital on January 21, 1952. Three and a half years ago she had begun to notice a nagging pain in the small of her back. This was followed by increasing pain in the hips and knees. About a year ago she had had burning pains in both legs, and her feet had felt numb and lifeless. Walking had become difficult, and eventually she had had to use two sticks. For a year her balance had been bad and she had had numerous falls, in spite of the sticks. She had not noticed that her legs were really weak until six months ago, when she found that she could not lift them up to get into a motor-car. Her left leg had had spasms, when it would cross over the right. She had had increasing trouble with her micturition for six months. Sometimes her water ran away without control and at other times she had great difficulty in passing it. At the time of admission she was getting about the house with difficulty. She had consulted Sir Robert Jones for bow legs at the age of 13.

On examination she was seen to be a short woman with marked bow legs. Her heart was moderately enlarged; her blood pressure was 130/65 mm. Hg. The jugular veins were not engorged. There were crepitations and rhonchi throughout both lung fields. Her ankles were not swollen, the liver was not palpable, and there were no clinical manifestations of any neoplasm. She had a moderate lower thoracic kyphosis with a slight scoliosis to the left. Apart from slight deafness the cranial nerves were normal. Both legs were very spastic, with adductor and flexor spasms that were severest in the right leg. All movements were present in the lower limbs, but the power was very poor. There was a pronounced level of hypalgesia to all forms of sensation at L 1. This faded off and there was hypalgesia at T 8 on the right and at T 11 on the left. Vibration was absent over the spinous processes up to T 10. The lower abdominal responses were absent but the upper ones were present. The tendon reflexes in the legs were exaggerated, but no clonus was obtained. Both plantar responses were extensor.

The blood picture was normal. Serum alkaline phosphatase was 12.8 units. Lumbar puncture showed a pressure of 120 mm. H_2O with a slight rise to jugular compression. The fluid contained 10 polymorphs per c.mm. and 80 mg. of protein per 100 ml. *X*-ray examination showed: fine osteolytic stippling of the skull; minor congestive changes in the chest; increased size of heart as in pulmonary heart disease; a mixture of sclerosis and osteoporosis of T 9 and 10 with slight collapse, and similar changes at L 3 (? osteitis deformans, ? secondary carcinoma); normal lower limbs. A myelogram from below showed a complete block at T 11.

Operation. This was performed on January 24 (anaesthetist, Dr. J. Ritchie). To supplement the general anaesthesia, hexamethonium bromide was used as a hypotensive agent. A low thoracic incision was centred over T 10 and 11. In separating the muscles there were numerous small blood vessels passing from the muscles to the bone that had to be controlled. The laminae and spines of T 9 and 10 were massive. The laminae of T 9 and 10 were completely removed and part of those of T 8 and 11. The thick bone was soft and very vascular. When the bone had been removed it was obvious that there was a small kyphus with its apex at T 10. The spinal theca was opened and appeared commodious. There was no evidence of any tumour, and it was possible to pass a fine rubber catheter for 8 in. (20 cm.) upwards and downwards without any difficulty. The dura mater was sutured and the wound closed in layers. It was not necessary to give a blood transfusion. The pathological report (Dr. R. Rodda) on the removed bone showed the typical changes of osteitis deformans.

After the operation there was slow improvement. When discharged home on April 2 the patient was able to walk but still used two sticks; bladder function was normal; tone of both legs was normal and the power slightly reduced; pain and temperature were felt everywhere; cotton-wool sensation was diminished in both feet; vibration was absent up to the anterior superior spines; position sense was very deficient in the ankles and toes; knee- and ankle-jerks were increased; the abdominal responses were all present; the plantar responses were extensor and there was knee and ankle clonus in the left leg.

When re-examined on June 5 she was walking well and used only one stick. Movements of the knees were still a little weak, the left more than the right. There was a trace of ataxia in the left leg. Vibration was absent in both lower limbs, but all other forms of sensation were normal. The right plantar response was flexor and the left extensor. Moist sounds were heard all over the chest.

Case 2

A man aged 65 was seen in consultation on October 16, 1951. In 1941 he had had an attack of congestive cardiac failure. At that time it had been noticed that he had an advanced osteitis deformans of the skull and spine. During 1945 he was admitted to hospital again, complaining of difficulty in walking. It was noted that both legs were weak and ataxic. All forms of sensation were poorly appreciated in the legs. The knee-jerks were absent and the plantar responses were flexor. By 1947 the weakness of his legs had increased and there was bowing of the right femur. *X*-ray films of both thighs showed severe osteitis deformans. He was fitted with a spinal brace. In 1949 he was admitted to hospital with retention of urine. The prostate was normal to palpation. Cystoscopy showed a fibrous bladder-neck and marked sacculation of the bladder. His bladder function improved and no active treatment was given.

He was again admitted to hospital in 1950 with urinary retention, and a transurethral resection of the prostate was done. A microscopical examination of the fragments showed senile hyperplasia. In spite of the resection he continued to have difficulty in passing his water. In the previous six months his leg weakness had rapidly increased and he had become bedridden. He had frequent attacks of breathlessness.

On examination he had a noticeably enlarged head and a very big right femur. His spine was rigid and there was an upper thoracic kyphosis. He had paraplegia in extension and was not capable of any voluntary movement in the legs. There was a marked hypalgesia to all forms of sensation to T 11. The abdominal responses were absent. The plantar responses were extensor and there was bilateral ankle clonus. His bladder was palpable at the umbilicus. The blood pressure was 200/100 mm. Hg, and the apex beat of the heart was felt 1 in. (2.5 cm.) outside the nipple line. There was considerable oedema of both ankles and he had severe dyspnoea on slight exertion. *X*-ray examination at that time showed gross osteitis deformans of the right scapula, pelvis, femurs, lumbar spine, thoracic spine,

and tarsal bones. There was left ventricular enlargement. A diagnosis of paraplegia due to osteitis deformans of the spine was made. In view of his poor condition he was regarded as unfit for laminectomy, and a gloomy prognosis was given.

He was seen next on August 28, 1952. There had been some improvement in his general health. He no longer had attacks of breathlessness, although his ankles swelled intermittently. He had not walked for about eighteen months. He was able to pass water, but it often leaked away, and there had been attacks of cystitis. Both legs were painful and his buttocks were uncomfortable. He had noticed that his head was still getting bigger and that his dentures no longer fitted. He was a permanent inmate of a "chronic" hospital.

On examination his blood pressure was 220/120 mm. Hg, and the apex beat was felt 1½ in. (3.8 cm.) outside the nipple line. There was no evidence of any congestive cardiac failure. His bladder was palpable at the umbilical level. He had a marked upper thoracic kyphosis. His head was big and the right femur was massive. There was a complete paraplegia in extension. There was considerable hypalgesia for all forms of sensation to T 7 on the right and to T 11 on the left. The abdominal responses were absent and the plantar responses were extensor. Fresh *x*-ray films showed that the disease had progressed and that the lumbar spine was ankylosed. The cervical spine was normal. Further, many ribs and the tibiae and fibulae were affected.

The paraplegia was of such long standing that little could now be expected from decompression of the spine. The cardiovascular reserves were small and so no operative treatment was advised.

Literature

In 1877 Sir James Paget described the bone disease that bears his name. Thereafter sporadic cases were recorded in which neurological symptoms had complicated osteitis deformans. Wyllie (1923) gave the first verified account of spinal-cord compression due to osteitis deformans of the spine. Kay, Simpson, and Riddoch (1934), besides having had two cases of paraplegia in 34 cases of osteitis deformans, had seven other cases with less severe neurological signs. Schwarz and Reback (1939), Turner (1940), and Teng, Gross, and Newman (1951) have surveyed the literature. The total number of published cases was 37. Further cases have been published, and Petit-Dutaillis (1951) gave details of three cases treated operatively. Fairburn (1951) had a case in which symptoms recurred after successful laminectomy and which was improved by further operation. Godlewski (1948) had a case of cervical spinal-cord compression successfully treated by head traction with skull callipers. With the above two instances, the total number of published cases of compression of the spinal cord due to osteitis deformans is 44.

Discussion

Teng *et al.* (1951) gave the incidence of paraplegia as 1 out of 131 cases of osteitis deformans, on hospital admissions. The true incidence would be much less, as osteitis deformans is diagnosed commonly without recourse to hospital admission. Gutman and Kasabach (1936) found 59 cases of osteitis deformans in the wards and out-patient department of a hospital that treated 200,000 new cases in the same period. Some cases were symptomless and the radiological changes were found in the course of examinations for other conditions. Osteitis deformans occurs equally in the two sexes (Kay *et al.*, 1934; Gutman and Kasabach, 1936). Spinal complications have usually been recorded in males. Case 1 is exceptional in being female, and is the fourth such case. The age spread has been from 36 to 77 years, with a maximum incidence in the sixth and seventh decades. In the spine, Paget's disease is most frequent in the lumbar vertebrae and then in the thoracic vertebrae; affection of the cervical spine is uncommon (Gutman and Kasabach, 1936). Paraplegia develops mainly in patients with thoracic spine involvement. Wyllie (1923) showed that there was an overall enlargement of all components of the vertebrae with the exception of the spinal canal. This was consistently narrowed. The most frequent site for the paraplegia was in the upper half of the thoracic spinal cord. Schwarz and Rebach (1939) indicated that, for the whole spine, the interpeduncular spaces were narrowest between the third and tenth thoracic vertebrae. There is the additional factor of a kyphus due to collapse of the softened body of the vertebra. This is well shown in Case 1, in which the spinal-cord compression occurred at the apex of a small kyphus. The vertebrae affected were the ninth and tenth thoracic, which is lower than usual. The roominess of the lumbar spinal canal is the reason why narrowing in this area rarely causes nervous signs. Case 1 had incidental involvement of the third lumbar vertebrae, but a rubber catheter was able to pass this site without difficulty. It is rare for the whole of the thoracic and lumbar spines to be affected, as in Case 2. The ultimate fusion of the adjacent vertebrae occurs when the intervertebral disk is replaced by the pathological bony process (Turner, 1940).

The usual history is of a slow and persistent interference with the functions of the spinal cord. The onset is insidious, and may be masked by the pains and failing mobility that characterize many cases of osteitis deformans. The duration of symptoms has been a year in most cases. Both of the above cases had long histories; in Case 1 it was three and a half years, and Case 2 had had osteitis deformans for seven years and neurological symptoms for six of them. Otherwise the progression of symptoms was typical in both cases. It was unfortunate that more attention was not paid to the nervous system in Case 2 when the bladder symptoms became troublesome. There are no special features of the spinal-cord compression except for the predilection for the upper thoracic segments.

The radiological features of osteitis deformans are well known. In Case 2 the emphasis was on an osteoporotic expansion of the many bones involved. There was radiological evidence that the whole lumbar spine was ankylosed. It may be difficult to differentiate the localized form of osteitis deformans from secondary deposits due to cancer. In Case 1 there was a combination of a sclerosis and a porosis with expansion of the pedicles, arches, and spinous processes of the affected vertebrae. On radiological grounds a carcinomatosis of the spine could not be excluded.

The condition most likely to cause confusion in the diagnosis is a benign spinal-cord tumour. Infective processes and malignant tumours cause a more rapid disintegration of nervous function. Turner (1940) pointed out that usually it was not the clinically obvious case of osteitis deformans that developed paraplegia. Although there may be evidence of a widespread bony involvement on radiography, the radiological features are typical enough to make the diagnosis reasonably certain. The presence of deafness is an additional diagnostic feature in many cases. All the clinical evidence in Case 1 pointed to a non-tumorous cause, in spite of the radiological uncertainty. While Case 2 has not been confirmed operatively, the long history and the affection of so many bones leave little doubt that the paraplegia is due to osteitis deformans of the spine. Among the recorded cases of paraplegia due to osteitis deformans the association of this condition with a benign spinal-cord tumour does not seem to have been made.

The only satisfactory form of treatment is removal of the affected spinous processes and laminae of the vertebrae. Myelography is desirable as a pre-operative measure, to confirm the level of compression and to exclude another lesion. When many vertebrae are implicated it may not be expedient to do an extensive laminectomy, and myelography would show the site of compression. The laminectomy can be very bloody owing to the vascular nature of the diseased bone. These patients come into an age group in which cardiovascular and respiratory diseases are

common. Osteitis deformans is associated with a special form of heart failure due to high output (Edholm, Howarth, and McMichael, 1945). The results of laminectomy depend on the duration of symptoms, and little improvement will occur when the paraplegia has been present for a long time. Out of the 44 cases in the literature, laminectomy was done 25 times, with three (12%) deaths, and 18 cases have shown improvement after surgery. An important complication is the recurrence of the paraplegia after the initial relief. This has happened in at least three cases.

Case 1 had chronic bronchitis and pulmonary heart disease, but she tolerated the operation well. Her recovery from the paraplegia was slow, but at the end of five and a half months she had only slight neurological deficiency. Case 2 was not operated upon when first seen, owing to his congestive cardiac failure and poor general condition. It was surprising to find him alive ten months later. Although his cardiovascular state has improved, he has been bedridden for eighteen months. It is extremely unlikely that any improvement in his paraplegia would occur if decompression was done at this date. The general risk is considerable and it has been decided that he should not be submitted to operative intervention. Sarcomatous change is a real contingency that cannot be obviated.

Summary

Two cases of paraplegia due to osteitis deformans of the spine are described.

The literature is brought up to date.

The differences between the two cases and the general pattern of the disorder are discussed.

I am grateful to Dr. John Willis, of Palmerston North, for referring Case 1 and to Dr. Ian M. Macgregor, medical superintendent, Silverstream Hospital, for access to the clinical notes of Case 2.

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The results of the first real test of the Emergency Bed Service's warning system are considered in the report of the service for the year ended March 31, 1953. The year under review includes the great London fog of last December, which resulted in a quite unprecedented rush of applications, and this was followed at the end of January by the influenza epidemic. Throughout this time of crisis, the warning system worked remarkably well, but the report says: "Although an outstanding success, experience has shown, however, that improvement is possible. At present the issue and cancellation of the warnings is solely dependent on the admission rate, and the winter has shown that this tends to result in the warning being put on rather too late and taken off too early. A modification of the scheme is being worked out whereby account is taken not only of the admission rate, but also of the number of applications being received and of the number of admissions made only after referring the case to the medical referees." Applications over the year as a whole increased, and analysis tends to confirm that this was owing to a rise in sickness rather than in the number of doctors using the service. The report also contains numerical details of the applications and admissions during the year.

RECURRENT GALL-STONE ILEUS

BY

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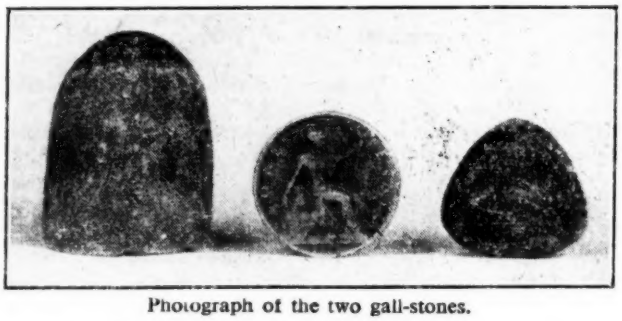
Gall-stone ileus is stated by various authorities to be the cause of 1–2% of all intestinal obstructions (Illingworth and Dick, 1941). Vick (1932) found that in over 6,000 cases of intestinal obstruction 0.68% were due to gall-stones. The high mortality, said to be over 50%, is due to delay in diagnosis and to the advanced age of the patients. Few of the reported cases were diagnosed pre-operatively. Several cases have been reported with multiple stones in the small intestine, but in only a small minority has a second intestinal obstruction occurred. Maurice Lee reported such a case in 1945. The stone usually ulcerates through between the gall-bladder and the duodenum, where it passes down into the small intestine, becoming impacted at the lower ileum. Wakefield, Vickers, and Walters (1939) in 141 post-mortem examinations found the fistulous track in 101 cases.

Case History

A housewife aged 57, 1 para, was seized by violent epigastric pain followed by vomiting two days before admission. These symptoms soon eased but returned on the day of admission, the pain this time being colicky in nature and central in situation. It was associated with severe and persistent vomiting. There was no relevant previous history apart from a dislike of fatty foods.

On examination the patient was dehydrated, with a dry, furred tongue. The abdomen was slightly distended, and on auscultation continuous loud peristaltic sounds were heard. Two enemas were given with negative results. After a diagnosis of acute intestinal obstruction of unknown causation, a laparotomy was performed.

First Operation (J. A. M.).—A distended loop of small bowel presented itself through a right middle paramedian incision. This loop contained a gall-stone which was impacted about 2 ft. (60 cm.) from the ileo-caecal valve. As it was too hard to crush, it was milked up into the distended loop and removed through a longitudinal incision. No other gall-stone could be felt in the small intestine. The gall-bladder area was not examined. Up till the ninth day the post-operative course was uneventful. The patient was taking nourishment and her bowels were working normally. On the tenth day, however, she complained of epigastric pain and vomiting. During the following 10 days she had attacks of incomplete intestinal obstruction, with colic, vomiting, and constipation one day followed by the passage of diarrhoea and flatus the next. It was thought that she had a post-operative obstruction due to local peritonitis and kinking, and attempts to relieve it by intestinal decompression were made. By the twentieth day it was decided that as she was not improving a further laparotomy should be performed.



Photograph of the two gall-stones.

Second Operation (Mr. W. J. M. Brandon).—The abdomen was opened through the previous wound. A second much larger stone was removed from the same area as before. The post-operative course this time, though slow, was uneventful.

The first stone was pyramidal in shape, faceted at its base, and 1 in. (2.5 cm.) in diameter. The second stone was shell-shaped and 1½ in. (3.8 cm.) in diameter (see photograph).

Comment

In this case the stones must have been lying silent for some time in the gall-bladder, the smaller stone ulcerating through first, the larger one taking 10 days longer to force its way through the preformed fistula's track. If the significance of the large facet on the base of the first stone had been realized, an earlier diagnosis of the post-operative symptoms could have been made. Both these stones were radio-opaque, as tested post-operatively. This is unusual. The sex of the patient, the lack of previous history, and the intermittent type of intestinal obstruction are typical features of this condition.

Summary

A case is reported in which 20 days after an operation for gall-stone ileus a second stone was removed from the small intestine. The patient eventually recovered.

I would like to thank Mr. W. J. M. Brandon, consultant surgeon, Law Hospital, for his help and permission to publish this case.

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Medical Memorandum

Mercuric Chloride Poisoning Treated with Dimercaprol

Mercuric chloride poisoning with suicidal intent is fortunately no longer fashionable in this country, although it still seems to be common on the Continent and in America. While Longcope and Luetscher (1949) in America reported on 61 cases of mercuric chloride poisoning treated with dimercaprol (B.A.L.), collected over a period of three years, no reports have, to my knowledge, been published in this country. It therefore seems of interest to make known the following case.

Case Report

A man aged 37 swallowed 2 g. of mercuric chloride with suicidal intention at 1 a.m. on May 6. He vomited repeatedly shortly after taking the tablets, but the vomit is said not to have contained solid particles of the substance, but only to have been stained blue. About one hour later he passed a large amount of pale urine and began to have cramps in his hands and feet. At 10 a.m. he had violent abdominal colic with bloody stools. He then took fright and sent for a doctor. He was admitted to hospital one hour later.

He was seen to be a rather underweight man of slender build, but there was no evidence of shock and no gingivitis; the tongue was coated but not dry. The pulse was regular and the blood pressure 110/80. The bladder was not palpable suprapubically, but no urine had been passed since 2 a.m. He complained of some abdominal colic and of painful cramps in his limbs.

He was given an immediate injection of 100 mg. of dimercaprol, and two hours later a further 200 mg. The injections were repeated at four-hourly intervals for four doses, and then 100 mg. was given four-hourly for a further four doses. The patient reported very shortly after the first injection that the cramps in his limbs were abating and he had no abdominal colic and no bloody stools.

The first specimen of urine was obtained at 10 p.m. in scanty quantity and loaded with protein; the sediment contained casts in most unusual numbers, some hundreds to a field. Next day the patient felt comfortable. His blood pressure was 120/70. The urinary output was still scanty and showed gross proteinuria, and blood urea was 46 mg. per 100 ml. The urinary output increased considerably from the third day, but there was a heavy trace of protein in the urine up to May 11. His blood pressure was stable at 120/70. On May 15 the sediment still contained a few casts. The patient was allowed up, and was discharged home on May 19.

The total dose of dimercaprol given was 1.6 g. over a period of 72 hours.

Comment

Although early vomiting may have prevented full absorption of the dose taken, it is likely that the consequences would have been fatal without appropriate treatment. Among a series of 86 cases of mercuric chloride poisoning reported by Longcope and Luetscher (1949), without treatment with dimercaprol, there were 27 deaths: death occurs in most cases of poisoning with 1 g. and more of the compound. Suppression of urine after an early diuresis, and bloody diarrhoea, point to a heavy absorption of the poison.

Following on the original publication by Peters *et al.* (1945) on the value of dimercaprol in the treatment of arsenical poisoning, Waters and Stock (1945) pointed out its possible use in the treatment of poisoning with other heavy metals, including mercury. Further, Gilman *et al.* (1946) investigated experimentally in cats and dogs the protective action of dimercaprol in poisoning with mercury, and reported favourably on it. The first and most important contribution to human therapeutics was by Longcope *et al.* (1946). They treated 23 cases of mercuric chloride poisoning with one death; one patient who recovered had swallowed 20 g. of the poison. Longcope and Luetscher (1949) reported a further 38 cases so treated, with only one other death. The dosage recommended by them is of 300 mg. for the first injection and a further two or three injections of 150 mg. at four-hourly intervals. A very important point is that treatment should be started at the earliest time within two or three hours from taking the poison. The one death reported occurred when treatment was delayed until 13 hours after poisoning.

Dimercaprol is known to produce toxic symptoms itself if given in a dose of 5 mg. and over per kg. body weight. These symptoms comprise nausea, vomiting, headaches, generalized aches and pains, burning sensations in the mouth, nose, and eyes, sweating, restlessness, weakness, and pains in the limbs, jaws, and trunk muscles. The heart rate is often increased, and there may be a rise in both systolic and diastolic blood pressure. These signs and symptoms subside within four hours (Peters *et al.*, 1945). The initial dose of 300 mg. recommended by Longcope may be expected to produce toxic symptoms in a number of patients of rather slender build; these symptoms have not been reported in the treatment of acute arsenical and mercuric poisoning, perhaps because the drug combines very rapidly within the body with heavy metals and is no longer available in free form. In comparison with the extreme danger to life of poisoning with mercuric chloride the risk of toxic reaction from the first large dose of dimercaprol is certainly inconsiderable.

The case described above made a remarkable recovery, as treatment was delayed for 12 hours and the first dose of the antidote was inadequate.

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Reviews

TEXTBOOK OF DERMATOLOGY

Dermatologie. By Professor Robert Degos. (Pp. 1,160; 301 figures. 8,600 francs.) Paris: Editions Médicales Flammarion. 1953.

This is an outstanding book in the great French tradition. It is comprehensive, but throughout bears the stamp of personal observation and experience. Many of the verbal descriptions are masterpieces, and these are supported by black-and-white pictures which are uniformly of the highest class both in photographic technique and in portrayal of their subject. The photomicrographs of histological sections are of equal calibre. Where required there are concise discussions in small print of the more scientific aspects of pathogenesis—for example, the relation of heparin to mast-cells, and the chemical aspects of melanogenesis. More attention is paid to foreign contributions to dermatology than in many French books, but though the author has read widely he has also read critically. Nowhere is the sense of personal experience more marked than in the sections on treatment, where the author's comments help the reader to determine which treatments are of actual rather than theoretical value. One might even wish that the author had had the courage to leave out some of those rather speculative forms of treatment which he obviously feels do not work in practice. He critically assesses such recently introduced agents as A.C.T.H. and the antibiotics, though he does not mention mepacrine in the treatment of lupus erythematosus. The whole book is beautifully produced on excellent paper, and bound in a stout loose-leaf cover so that supplementary pages may be added from time to time.

With such an excellent production it seems almost churlish to criticize, but it is hoped that anything which is said here may be construed as constructive and not destructive. The arrangement in chapters is based purely on the descriptive nature of the lesion—for example, erythematous lesions, papular lesions, scaling lesions, etc. —and the book suffers from defects inherent in such a system. Thus observations on syphilitic lesions are scattered throughout at least eleven different chapters, which entails many cross-references, while accounts of such varied conditions as warts, urticaria, Darier's disease, and filariasis are all found in one chapter. Even this system breaks down, and the author is forced to have such chapters as "Malignant Haematodermia" and "Naevi" which do not conform to one type of clinical lesion. It would surely be easier for the reader and make for clearer thinking if the book were arranged aetiologically, even though some difficulties might result. The other major criticism is that the book does not convey to the reader the importance of psychological factors in many dermatoses. There are references to "chocs émotifs" and "troubles nerveux," but these are only in passing, and no account is given of such fundamental work as that of the Guy's school on the asthma–eczema complex or Klaber and Wittkower on rosacea. In patients with constitutional eczema no mention is made of psychological treatment either by a sympathetic dermatologist or a trained psychologist, nor of phenobarbitone.

Other omissions noted are any reference to thorium X, or to dithranol in the treatment of psoriasis, nor is any mention made of cholinergic urticaria and Grant's work, nor of recent work by O'Brien and Sulzberger and others on prickly heat. The proof reading in French has been excellent, only one slip being noticed (*naïéance* on p. 445), but, though better than most French writings, English names are still spelt wrong, even "Whitefield," and there are several examples of unusual accentuation—e.g., pemphigus érythématosus (p. 445).

But these are trivial points in what is undoubtedly one of the best textbooks of dermatology produced in any language for many years.

F. F. HELLIER.

EXPERIMENTAL HYPNOSIS

Experimental Hypnosis: A Symposium of Articles on Research by many of the World's Leading Authorities. Edited by Leslie M. LeCron. (Pp. 483. $6 or £2 5s.) New York and London: The Macmillan Company. 1952.

In the numerous recent books on hypnosis, it is presented variously as a method of treatment scorned by orthodox medicine and offering new hope for suffering mankind, as a mystery exclusive to master minds, as a sort of back door to the occult world, or as a branch of medicine meriting a Royal Society of its own. The drama of the hypnotic séance has been apt to get into the writer's style, and he presents himself either as a high priest in triumph or as a misunderstood man who has to appeal to the layman for a fair hearing.

The editor of this book has succeeded in avoiding these difficulties and in marshalling 20 contributors who present, for the most part, objective evidence, much of it original, on aspects of hypnosis which can be subject to experiment. Experiments on different techniques, the state of the nervous system at different levels of hypnosis, its effects on memory and efficiency in mental tests, on the time sense, on the formation and extinction of conditioned responses, and on autonomic and secretory function are all discussed. There is a reasoned appreciation, supported by experiment, of the possibilities of misuse of hypnosis for antisocial ends and an account of the results of its use in dentistry and obstetrics. Particular interest attaches to the editor's own work on age-regression and the results of educational tests given to subjects who have been told they are of school age.

All books on hypnosis have a lay circulation, especially among the morbidly interested, and the authors recognize this. But they discuss the sort of questions which are commonly asked by the intelligent and stable layman and the medical research worker, and give a general view of the present state of experimental work in a readable form. Continuity between the contributors is provided by a foreword to each article by the editor, who has produced a book of great interest to the general medical reader.

ALEXANDER KENNEDY.

TEXTBOOK OF GYNAECOLOGY

Textbook of Gynecology. By Emil Novak, M.D., D.Sc. (Hons.), F.A.C.S., F.R.C.O.G.(Hon.), and Edmund K. Novak, M.D., F.A.C.S. Fourth edition. (Pp. 800; 522 illustrations. £3 8s. 6d.) London: Baillière, Tindall and Cox. 1952.

In writing this fourth edition of his textbook of gynaecology Dr. Emil Novak has enlisted the help of his son, Dr. Edmund K. Novak. If this is a sign of advancing years and preparation for retirement on the part of the senior author, the book itself shows no such signs. It remains distinguished by the charm, enthusiasm, fluency, and well-ordered knowledge of the master. Some may argue that the pattern is more orderly than Nature intended or indeed shows, but the examination candidate will not have any such misgivings and will be thankful to have all scientific doubts and discrepancies disguised or hidden away.

Anyone meeting this book for the first time and without its title page would have no difficulty in recognizing it as written by the author of *Gynecologic and Obstetric Pathology,* which was first published one year earlier. The two books are similar in style and layout, and many of the illustrations are identical. This is considerably larger because, in addition to the systematic accounts of various diseases and their pathology, it includes many chapters on essentially clinical problems such as menstrual disorders, sex and marital relations, discharge, backache, sterility, and endocrine upsets. A chapter on female urology is contributed by Dr. H. S. Everett.

Since the book is designed for undergraduates and general practitioners, all details of surgical treatment are deliberately and properly omitted. Many undergraduates will probably consider that for their purposes the other aspects could well have been abbreviated. But more

advanced readers will find the book extremely attractive, and, except for those interested only in pathology, it is rather better value than its elder sister, for it contains nearly as much pathology and much more besides.

T. N. A. JEFFCOATE.

HISTORY OF NEUROLOGICAL SURGERY

The History and Development of Neurological Surgery. By Ernest Sachs, M.D. (Pp. 158; 50 figures. £1 10s.) London: Cassell and Co. 1953.

This is a very brief account of the development of neurological surgery from the earliest times to the present day. The first half of the book is on the interesting but relatively unimportant surgical measures undertaken from the earliest times to the advent of the Listerian era; into the second half are crowded all the remarkable advances made during the past hundred years. The reader will probably wish that the author had expanded the latter half to twice or three times its present size. Nevertheless, by the inclusion of 540 references, the way is left clear for anyone to follow up any particular subject in which he is specially interested.

Due credit is given to the outstanding pioneer work of Victor Horsley and Harvey Cushing, but we thought it inaccurate to attribute to the latter the devising of the transfrontal method of approach to the pituitary fossa. Frazier, by modifying MacArthur's technique, first popularized the transfrontal approach, though no doubt Cushing modified the details of the method.

It is well said that during the war of 1939–45 neurological surgeons for the first time came into their own, and that in that war results of treatment of head injuries were far better than ever before. If the author had compared mortality from penetrating head wounds in the first and second world wars the figures would have been most impressive, for it is known that the mortality was reduced from 50% to less than 10%. Half a page is given to a description of the improvement in the treatment of spinal injuries, but there is no mention of the remarkable work of Ludwig Guttmann, whose ingenious and active methods of rehabilitation have revolutionized the outlook for many of those who were formerly left to linger on in misery until death relieved them.

The book is illustrated by fifty attractive illustrations. On p. 36 occurs the word "escerotics" where the sense demands "escharotics," and the curious word is repeated in the index. We thought this might be an American form of the more common term, but could not find it in an American dictionary and must presume it is a misprint.

ZACHARY COPE.

BONE TRANSPLANTING

Die Konservierung von Knochengewebe für Transplantationen. By Hans Roth. (Pp. 222; 233 figures. £4 3s.) Vienna: Springer. 1952.

An active field of research is at present provided by studies on the behaviour of tissues and organs transplanted from their normal site, or from one individual to another. Interest in the subject is stimulated by hopes of widening the scope of the surgical use of grafted tissues in the replacement of anatomical or physiological defects in the body. Blood transfusion is a frequently employed transplantation, while such tissues as skin, corneal tissue, bone, cartilage, blood vessels, and endocrine glands are being used or studied, and the possibility of grafting intact organs, such as the kidney, is under active investigation.

The author of the present volume, a surgeon of the university clinic at Basle, discusses in some detail the preservation of bone tissue for transplantation. This is prefaced by a good general account of the behaviour of bone transplants as seen in experimental studies. The author summarizes most of the important work in this field, and in addition describes experimental studies of his own. He also recounts his extensive experience with clinical bone grafts and with the organization of a "bone bank" for the preservation of the necessary grafting material.

Innate chemical and immunological differences appear usually to prevent more than the transient survival of cells when transplanted from one individual to another, and it is of interest that the regular and effective use of bone as a grafting material depends on factors other than cell survival on the part of the transplant. Indeed, bone now has to compete with a range of non-biological synthetic substances as a grafting material, and its advantages depend chiefly on its influence as a stimulus to the development of new bone by the tissue in contact with the graft. Grafted into the skeleton, the ultimate fate of a satisfactory transplant is complete replacement by newly developed living tissue which becomes functionally incorporated into the structure of the bone.

The healing process is much the same whether the transplanted bone comes from the individual into which it is grafted, from another individual of the same species, or even from a different species. Available information suggests, however, that the rate of repair is more rapid when the graft is an "autotransplant," but the convenience of using "preserved" bone from another individual is such that this type of graft (that is, a "homotransplant") finds frequent clinical use.

After his account of general studies with experimental transplants the author outlines the technique he has developed for the operation of a "bone bank" and for the clinical use of the material from it. He uses corpse bone, removed with aseptic precautions and preserved by refrigeration in liquid paraffin at a temperature of about −15° C. Dr. Roth has used such material on more than 100 occasions in a wide variety of orthopaedic operations.

This book is accurately written and excellently produced, with an index and a good bibliography. It is certain to be of considerable interest and use to those concerned with any aspect—clinical or experimental—of bone transplantation.

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TREATMENT OF BURNS

On Burns. Compiled and edited by Nathan A. Womack, M.D. (Pp. 178. £2.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953.

This book is the story recorded on tape and "gently edited" of a 1½-day conference held in the State University of Iowa in 1951. As an authoritative work on the treatment of burns it is disappointing, though as a detailed record of a good conference between surgeons and research workers it is admirable.

The only clinical material carefully analysed is a study of 200 severely burned patients treated in one hospital from 1930 to 1950. This was a period of great change in methods of treating these injuries, and relatively few of the 200 had been treated by accepted modern methods. One contributor, Dr. Truman Blocker, is an obvious enthusiast for exposure treatment of acute burns, but the argument and evidence he presents for this method are not altogether convincing. His chapter might well have been matched by an equal enthusiast for a carefully undertaken occlusive method of treatment, but the book contains no authoritative evidence on this matter, nor does it indicate that both methods have their place in local treatment. The conference discussed most of the important problems associated with the treatment of thermal injury in peacetime, and it will be of interest to all who are concerned in this.

The symposium was an outgrowth of a discussion of a State Advisory Committee for Civil Defence, concerned with stock-piling material for the medical care of thermal injuries in any future war with modern weapons. It sought only to get a clearer understanding of accepted hospital methods of handling thermal injuries. The main value of the book to readers in Britain is that it is an excellent example of a realistic approach to a civil-defence problem by the State of Iowa, an example that could well be followed by the regions and their hospital authorities here.

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MENTAL ILLNESS IN TWINS

Mental illness has to-day yielded relatively few of the secrets of its more common forms, and, though the theory of demoniacal possession and the wages of sin may have given place to dianetics and the importance of guilt-feelings, the proportion of theory to observation is often still very high. The only antidote to this is sound observation, and for those who can tolerate the pains of scientific doubt the unsolved problem of the major psychoses has acted as a stimulus to the gathering of reliable information, to consideration of predisposing and exciting causes, and to planned observation of the natural history of the morbid process. In this respect the progress of research into schizophrenia and cancer—to take two common diseases—is remarkably similar; there are advances in empirical treatment and accumulation of much information, but the main problem awaits solution. In both the constitutional approach has led indirectly to advances in the science of genetics, because it was a necessary preliminary to establish the extent to which inherited factors could predispose to disease and the extent to which a morbid predisposition could be modified by factors occurring during life and by the effects of treatment. In the same way, also, it has been necessary to investigate genetic factors in normal tissue growth and, in the study of the mental disorder, the inherited factors in the growth of normal personality, of which that of the schizophrenic is a caricature.

It is seventy years ago since Francis Galton[1] gathered information about the intellect, temperament, and character of twins and showed that identical twins were more alike in these respects than binovular ones or siblings of different age. In 1926 Dahlberg[2] reported his findings in a large number of normal twins and discussed the applicability of twin studies to the problem of hereditary and environmental influences. Since then a series of workers have successively brought new principles to light and developed new techniques in this specialized field of study.

If a pair of uniovular twins are separated at birth and brought up in different environments, and if both develop schizophrenia at the age of 17, one after an unhappy love affair and the other after working hard for an examination, it appears at first sight that a few more of such examples would make the evidence for a wholly genetic aetiology for the disease overwhelming. The matter is, however, not as simple as that, and it was Luxenburger[3] who pointed out how deceptive might be the conclusions drawn from the isolated reported case. While recognizing that such cases, selected because of exceptional interest, are of great value in indicating possibilities, he showed that they are of relatively small importance in estimating the general significance of inherited factors. For this reason he embarked on a study of unselected twins by collecting from hospitals over a large area of Germany the names of all the patients with schizophrenia who happened to be twins. Taking uniovular and binovular twins together, Luxenburger found that for every pair of twins in which schizophrenia appeared in both there were four pairs in which only one twin was affected—in other words, there was a concordance rate of 20% as against 80% in cases collected from the literature. But only uniovular twins can be regarded as genetically identical, and the later studies of Lange,[4] Smith,[5] and Rosanoff[6] on criminal, mentally defective, schizophrenic, and manic-depressive twins suffered from the defect that there was no satisfactory criterion of ovularity. Rosanoff made the important suggestion that separate gene-borne predisposing and activating factors might account for the irregular familial distribution, especially in manic-depressive states. In the later work of Conrad[7] and Stumpfl[8] the ovularity was more carefully investigated. In 1939 Juda[9] reported on a study of mental defectives and showed that conditions hitherto thought to be due to birth trauma occurred in both twins when one had been delivered without difficulty. In general the concordance for states of mental deficiency accompanied by physical stigmata was very close. A further advance was made in 1941 by Essen-Moller[10] in Sweden, who observed in a series of unselected twins that in schizophrenia especially there might be concordance in the fact of breakdown, but that the clinical picture sometimes differed very greatly in the pairs studied. In other observations, especially those of Kallmann,[11] the

1 *Inquiries into Human Faculty*. London, 1883.
2 *Twin Births and Twins from a Hereditary Point of View*. Stockholm, 1926.
3 *Z. ges. Neurol. Psychiat.*, 1928, **116**, 297.
4 *Verbrechen als Schicksal, Studien an kriminellen Zwillingen*. Leipzig, 1929.
5 *Z. ges. Neurol. Psychiat.*, 1930, **125**, 678.
6 *Amer. J. Psychiat.*, 1934, **91**, 247.
7 *Z. ges. Neurol. Psychiat.*, 1935, **153**, 271.
8 *Die Ursprünge des Verbrechens dargestellt am Lebenslauf von Zwillingen*. Leipzig, 1936.
9 *Z. ges. Neurol. Psychiat.*, 1939, **166**, 365.
10 *Acta psychiat. (Kbh.), Suppl.* 23, 1941.
11 *Congrès International de Psychiatrie, Rapport VI Psychiatrie Sociale* (pp. 1–27). Paris, 1950.
12 Slater, E., *Psychotic and Neurotic Illnesses in Twins, Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 278, 1953. H.M.S.O., London.

high concordance in both schizophrenia and manic-depressive psychosis was confirmed, and from his material it became clear that in spite of the great aetiological importance of heredity recovery may occur, and this may be related to treatment.

In 1936 Dr. Eliot Slater set out to plan a survey of unselected twins appearing in the London mental hospitals and psychiatric units, a study which would be free from the objections to previous inquiries and in which, for the first time, the relationship of normal personality to psychotic symptoms would be considered. He also included psychoneurotic disorders and psychopathic personalities in the scope of his inquiries. The results, now published as a monograph[12] by the Medical Research Council, represent the conclusion of an enormous task carried out with a constant appreciation of the dangers of loose thinking and of the need to compile records which would be of use to later workers in the same field. It is not too much to say that Dr. Slater, in working out his methods and presenting his results, has made contributions to this branch of study which are applicable throughout all medical research. Altogether there were 295 patients, born from multiple births, about whose twins the necessary information was collected, and a full clinical study was made of each pair. The greatest care was taken to establish ovularity, and an original method of converting finger-print characteristics into terms of figures was worked out and proved to be a reliable index of similarity. Attention was paid to personality traits as well as to the symptoms of psychiatric disorder, and the case histories were condensed into summaries without great loss of content. The results are clearly given, and the protocols are such that further results of interest will be obtainable in the future as specific problems are thrown up by later work.

Fortunately the results of Slater's consistent and dispassionate approach emphasize the great importance of environmental factors on individuals rendered vulnerable to disease by their heredity and show that they can be helped to adjust themselves to life in spite of the inborn handicap. This evidence should make those concerned with treatment less hesitant to face the facts of genetics, and less inclined to therapeutic pessimism when the constitutional element is clearly great.

Slater has also shown that, with certain limitations, research on twins, especially when combined with clinical studies, is a valid approach to the problem of heredity and environment in mental disease. So far as specific diseases are concerned, the concordance for schizophrenia in uniovular twins was 76% compared to Kallmann's 86%. From this it is deduced that heredity plays a major part in predisposition to this disease, but the case studies indicate that the personality of the individual and the experience of his lifetime have much to do with whether the disease becomes manifest or not. Among the psychopathic and psychoneurotic twins the concordance rate was lower, but the actual form of the disorder was more often similar—and this appears to be related to the strong evidence in this study that the basic make-up of the personality is largely determined by heredity. It will take some time to digest and apply the results of this survey, but there is little doubt that the Medical Research Council, in sponsoring this work, has assisted Dr. Slater to present a report which will doubtless rank as a classic in methodology and in the objective presentation of clinical material. It will, in addition, notably increase the ratio of observation to theory in the very speculative field of the aetiology of mental disorder.

FIRST WORLD CONFERENCE ON MEDICAL EDUCATION

Modern history may justify scepticism about the usefulness of large international gatherings, but those who had the duty of thanking the organizers of the First World Conference on Medical Education—held in London last week under the auspices of the World Medical Association—spoke with a sincerity which was clearly in tune with the feelings of the delegates. The 600 representatives who came to the Conference from 59 countries and 92 medical schools or universities seemed confident that medical teachers at least could disregard the barriers of distance and language and meet as one group of people with a common purpose—the improvement of the practice of medicine.

The results of a conference of this size cannot be quickly assessed and packed tidily away into compartments labelled "premedical studies," "preclinical studies," "clinical studies," and so on. In general the delegates had no difficulty in agreeing that changes were needed in medical education, but, as Dr. Victor Johnson remarked, it is easier to move a graveyard than change the curriculum. The course of medical study is like a slab of butter: it can be pressed into various shapes, and pieces lopped off at one end can be slapped on at the other, but the volume remains the same. The Conference heard many suggestions about the shape the curriculum should take and about the places where a reduction appeared possible and, more commonly, where additions were essential. No one had the temerity to

say that a perfect curriculum could be devised for any one country, let alone the world, but all were agreed that efforts to improve medical education should be unceasing—which seems to indicate that the first world conference on this subject will not by any means be the last.

In last week's *Journal* we commented on the purpose of the Conference and published Sir Lionel Whitby's presidential address and other papers read at the opening plenary session. Elsewhere in this issue we continue our report of the proceedings of the Conference (pp. 556 to 565)—a report that has necessarily to be curtailed, for over 200 speakers contributed to the discussions during the week. The final assessment of the work of the Conference will have to await the publication of its *Proceedings*, but there can be no doubt that it fulfilled the hopes of those who originated the idea. At the concluding plenary session the vice-presidents and rapporteurs of each of the four sections gave most thoughtful and informative reviews of the week's work, and their addresses will be reported in full in next week's *Journal*.

In the section which discussed "Requirements for Entry into Medical Schools," the case for educating prospective medical students in the humanities was of course put strongly, but, as Dr. Raymond Whitehead, the rapporteur of the section, pointed out in his remarks, the section felt it was worth emphasizing that education in science had its own cultural value—a view which those with no scientific training often conveniently ignore.

In this section the topic which provoked the most lively discussion was that on the selection of students. Plato thought that the ideal State should have a ruling caste nurtured and trained for government. The ideal medical student could be produced only by the same Utopian methods. Teachers are perhaps in danger of expecting too much from their students, and, as Dr. Whitehead said, they should be content to see only one or two divine attributes in them, remembering that "they are merely ourselves when young." The main purpose of selection is to pick out those who will educate themselves. The view that self-education was all important in the making of a doctor—both before and after graduation—was repeated time and again throughout the conference. A medical student from the Netherlands even went so far as to say that examination failures were often due to the fact that students were too hampered by their teachers and not allowed to find their own way about.

In his comments on the work of the second section—"Aims and Content of the Medical Curriculum"—the vice-president, Sir A. L. Mudaliar, wisely reminded his audience that the content of the curriculum matters less than those who teach it. There was no lack of constructive suggestions about how the teaching of some subjects—anatomy and physiology, for instance—could be combined and about how the whole curriculum could be integrated. Dr. Morgan Jones, the rapporteur of this section, called attention to the general feeling that the fragmentation of the curriculum must not be allowed to go any further and that the study of medicine must be made a comprehensible whole once again. There are many ways of teaching the basic sciences and of relating this teaching with clinical problems, but, as Dr. Morgan Jones summed it up, "for the study of the practice of medicine in its broader aspects, there is no substitute for clinical clerkships, out-patient clinical work, and the study of the patient in his home and occupational environment."

Medical educators, like all other teachers, must remain constantly aware that the road they are travelling can very quickly become rutted. Professor A. Hurtado, the vice-president of the section considering "Techniques and Methods of Medical Education" urged the importance of experimentation in teaching as in all medical subjects. Many interesting schemes which are being tried out in various parts of the world were described during the meeting of this section, and there was a lively discussion about the place of teaching in the patient's home. This reflected the general awareness of the danger that the student may come to regard a patient in a hospital bed as a case—interesting or commonplace—but there was agreement that teaching in the home should not be designed as a preparation for general practice any more than teaching in the hospital should be designed as a preparation for a specialist career. The aim of all teaching should be to turn out what one speaker described as "the basic doctor," who on qualification would be prepared to launch out into the study and, later, practice of that branch of medicine for which his inclination and talents fitted him. As Professor Hurtado said, it would be entirely erroneous to try to fit pregraduate education into some predetermined plan of postgraduate activity. This section agreed on the value of the clinico-pathological conference as a tool of medical education and heard several experts talk on the management of group discussions. In presenting his report as rapporteur of the section Professor Ian Aird said that at times it was essential for the teacher to descend from his lofty isolation and let his students argue and discuss, "merely correcting their errors and guiding the direction of their common flow of thought." Several speakers emphasized the necessity for close personal association

between teacher and student, but not much was said in debate about the tutorial system which Sir Lionel Whitby recommended in his presidential address. This entails the selection from among the teaching staff of "tutors" to guide the steps and supervise the work of a group of students. No doubt future conferences will return to this theme.

The fact that preventive and social medicine was allotted a section of its own at this conference may have occasioned some surprise, but, as Professor Stampar said, it also gave much satisfaction to those who have long believed in the importance of social medicine, not only as a subject in the medical curriculum, but also as a background to hospital and family practice. As a matter of fact speakers in every section seemed anxious to comment on the new slant which medicine was taking as the result of a more perceptive understanding of the relationship between health and social welfare. That social medicine still does not receive enough attention was a common complaint, but even those who agreed with this complaint were not too sure of the exact place of social medicine in undergraduate education. The influence of socio-medical studies is of course now pervading the whole curriculum, and this influence is bound to become stronger. Why, then, are some clinicians still hostile to this subject? Dr. Charles Fletcher, the rapporteur of this section, gave one possible answer to this question:

> "Experts in social medicine do not find it easy to expound their subject, which, though precise and objective in many aspects, also contains many conceptions that are still imprecise. Its advocates are thus tempted to talk in indigestible phrases, whose meaning, I suspect, is often as doubtful to them as to the rest of us. Such terms must be repressed if medical men are to listen, and social medicine must base its claims on a clear exposition of effective and comprehensible achievement."

It is only fair to add that contributors to the discussions of this section clearly showed that they possessed the powers of exposition which social medicine particularly demands.

When the Conference came to an end last Saturday no one doubted its success. Disagreements in debate were numerous, but there was no acrimony. The many social occasions, graced by the presence of the delegates' wives and families, were true demonstrations of international amity. Above all, there was an optimistic conviction that medical teachers, united by their strong professional bonds, common purpose, and humanistic tradition, could, and would, exert a strong influence for the good in world affairs.

DEFICIENCY OF POTASSIUM

The amount of potassium in the body, as measured by the technique of isotope dilution, is about 40 mEq. per kg., or some 2,800 mEq. in all.[1] The amount in the extracellular fluid, 4 mEq. per litre, is very small, and 97% of the potassium in the body is in the intracellular fluid. Potassium is normally lost through the skin, the bowel, and the kidney. The kidney can adjust to a very low intake,[2,3] though it may take a few days to do so, but a loss from the skin and the bowel, of the order of 10 mEq. daily, continues.[4] During starvation the potassium liberated by the breakdown of body tissues may be enough to cover the inevitable losses and to maintain a normal concentration in the body fluids,[5] though the total amount in the body is obviously reduced. On the other hand, moderate deficiencies of potassium may arise with artificial diets that exclude potassium but provide adequate calories and protein.[2,3,4] Mr. I. W. MacPhee discusses in this issue (p. 528) the mechanisms involved in the production of potassium deficiency. Large deficits, amounting to 30% of the total,[6,7] may occur when the losses from the body are abnormally large. This happens, for instance, when fluid is lost from the gastro-intestinal tract by vomiting, aspiration, or diarrhoea, or through a fistula; and also when the normal renal mechanism for conserving potassium is upset by acidosis[8] or alkalosis.[9] Some forms of renal disease themselves lead to large losses of potassium.[10] Moreover, perhaps because of an increase in the excretion of adrenocortical hormone, the renal conservation of potassium is not so efficient in ill persons as in the normal.

A deficiency of potassium may thus complicate many diseases, but symptoms attributable to it have been capricious in their incidence and have been relieved, at least temporarily, by doses of potassium that were small compared with the total deficit. For example, a deficit of 800 mEq. is equivalent to 60 g. of potassium chloride, but severe symptoms, if present at all, may disappear after the first dose of 10 g. The clinical effects depend partly on other changes in electrolyte metabolism as well as on the extent of the deficit of potassium. Potassium shortage is compensated by a retention of sodium in place of potassium

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2 Black, D. A. K., and Milne, M. D., *Clin. Sci.*, 1952, **11**, 397.
3 Lowe, K. G., ibid., 1953, **12**, 57.
4 Blahd, W. H., and Bassett, S. H., *Metabolism*, 1953, **2**, 218.
5 Aikawa, J. K., *Proc. Soc. exp. Biol. (N.Y.)*, 1951, **78**, 524.
6 Fourman, P., and Ainley Walker, K. M. S., *Lancet*, 1952, **2**, 368.
7 Schwartz, W. B., and Relman, A. S., *J. clin. Invest.*, 1953, **32**, 258.
8 Fourman, P., *Lancet*, 1952, **1**, 1042.
9 Franglen, G. T., McGarry, E., and Spencer, A. G., *J. Physiol. (Lond.)*, 1953, **121**, 35.
10 Milne, M. D., Stanbury, S. W., and Thomson, A. E., *Quart. J. Med.*, 1952, **21**, 61.
11 Cannon, P. R., Frazier, L. E., and Hughes, R. H., *Metabolism*, 1953, **2**, 297.
12 LeQuesne, L. P., and Lewis, A. A. G., *Lancet*, 1953, **1**, 153.
13 *New Engl. J. Med.*, 1952, **246**, 637.

in the cells and is associated with an alkalosis in the extracellular fluid,[3] shown by a high bicarbonate and a low chloride concentration in the plasma. Under these conditions symptoms may be slight, but if sodium is not retained and if there is a complicating acidosis symptoms may become obvious once the deficit of potassium exceeds some 10–15% of the total body potassium.[6] Mental apathy and stupor, anorexia, nausea, and symptoms of intestinal atony are among the more prominent. With very gross deficiencies such symptoms may occur even without a complicating acidosis, and Dr. J. S. Logan gives an instance elsewhere in this issue (p. 532). He suggests that a gastric ileus in his patient, who had had a gastro-enterostomy, may have been attributable to the deficiency of potassium.

The large amounts of potassium required to correct a deficiency cannot be given quickly because a sudden rise in the concentration of potassium in the extracellular fluid may stop the heart. Fortunately the urgent manifestations of a potassium shortage can be reversed with relatively small amounts of potassium, provided the compensatory mechanisms for a potassium deficiency can operate. Therefore if sodium deficiency and acidosis complicate the picture they must be corrected. A low plasma bicarbonate content points to the need for saline. Although urgent symptoms may abate with minimal treatment, it is still desirable to correct the potassium deficiency completely, for, even when compensated by sodium retention, it may cause myocardial lesions[11]; it may be responsible for apathy, anorexia, constipation, and intestinal atony in convalescent patients; and it may predispose to oedema.[6 12]

Normal diets provide 50–100 mEq. of potassium daily and will gradually restore a deficit. With smaller intakes or with continuing losses supplements of potassium may be needed, but, when possible, intravenous administration must be avoided. But when intravenous therapy is essential the amounts of potassium provided by Ringer's solution and the like are quite inadequate for the treatment or prevention of a deficiency. The usual practice is to give a solution containing 2.7–3.1 g. (70–80 mEq.) in a litre slowly *over four hours*. Logan points out that intravenous therapy may be avoided by giving potassium per rectum.

The ideal course of action is to prevent major deficiencies from arising in patients who are in danger. At present the diagnosis of potassium deficiency rests above all on the history of abnormal losses. The losses can, however, be replaced as they occur, and for this Cooke and Crawley[13] have devised two simple solutions for patients who are losing gastric or intestinal secretions. The appropriate solution is given intravenously in a volume equivalent to that lost. Surgeons may welcome this means of avoiding a difficult biochemical problem when patients are unable to take potassium salts by mouth.

A NEW ADRENAL COMPOUND

The various types of biological activity which reside in the suprarenal glands can be tracked down to their origins in certain chemical fractions, and from these concentrates 29 separate crystalline steroid substances have been isolated. The chemical constitution of all but one of these substances has been determined, and during the last year or so nearly all of them have been synthesized. Of these 29 compounds, about 7 have shown themselves able to prolong life in adrenalectomized animals and to prevent the occurrence of at least one of the major side-effects of adrenalectomy. When subjected to different methods of assay these seven key compounds have shown considerable differences in their main modes of action, which are, however, often roughly divided under the headings of "mineraloid" and "gluco-corticoid" activity. The most potent of the gluco-corticoids is hydrocortisone (17-hydroxy-corticosterone), and until now deoxycortone (D.C.A.) has proved itself the most active of the mineralo-corticoids. Corticosterone takes a half-way position between these two substances. So far, the two most potent of the gluco-corticoids, hydrocortisone and cortisone, have been recognized as being the substances whose effect on the pathological processes of rheumatoid arthritis and certain other rheumatic diseases is greatest. Nevertheless, it is recognized by clinicians that even for this purpose it is probable that more effective substances, or combinations of substances, may emerge as the physiology of the adrenal gland and its secretions become better understood.

Examination of blood from the suprarenal vein has shown that corticosterone and hydrocortisone are released from the gland in amounts which make it very probable that it is these two compounds which are responsible for the normal adrenal carbohydrate metabolism. On the other hand, similar observations have not supported the original idea that mineralo-corticoid activity is principally regulated by deoxycortone. It now seems that the steroid fraction which is mainly responsible for the mineraloid activity of the normal gland is a new compound, to which the name "electrocortin" has been provisionally attached by Simpson and Tait of the Middlesex Hospital Medical School. Since, however, this compound is contained within the "amorphous fraction" of the glandular secretion, it has previously been impossible to investigate the effect of this fraction on the human or animal body.

On August 25 Professor T. Reichstein, who in 1951 shared the Nobel Prize for Medicine with Drs. P. S. Hench and E. C. Kendall, announced at the Eighth International Congress of Rheumatic Diseases held in Geneva that he has been able at last to produce this

substance in pure crystalline form. The process of crystallization is at present long and complicated, and no doubt it will be some time before therapeutic trials of electrocortin can be started. The outlook, however, is promising, since it would appear that from now on the three main hormones of the normal adrenal cortex will be available in pure form, and clinicians will be able to administer them in controlled fashion, varying the relative dosage in accordance with the needs of the body. They may thus shortly be able to reproduce the normal functioning of the adrenal cortex in those diseases, including the rheumatic group, in which this form of therapy can be shown to be of major therapeutic importance.

SELECTION OF STUDENTS BY INTELLIGENCE TESTS

Sir Frederic Bartlett, who last week addressed one of the sections of the First World Conference on Medical Education on the use and value of intelligence and aptitude tests, threw aside his distributed paper, which was concerned with general and fundamental considerations, and made the first public statement on the results of a long-term investigation which the Medical Research Council set on foot a little more than five years ago on all aspects of the selection of medical students in Great Britain. A small research group was organized under Dr. A. D. Harris, with its headquarters in the experimental psychology laboratory in Cambridge. The initial plan contemplated a five years' study. The design was to apply representative tests of intelligence to a reasonably large population of prospective medical students before any of them had taken their first medical examination, then to follow these students through all their preclinical and clinical medical examinations to their first years in professional practice. The tests used were all of familiar type, fully meeting the usual conventional requirements, and of proved reliability. Complete results were now available, said Sir Frederic Bartlett, for a comparison of test performances with examination records in the first and second M.B. examinations. The conclusion was that the predictive capacity of tests of this kind for the first two medical examinations as conducted in this country was, with one possible exception, entirely negligible. They could, as the situation stood at present, add nothing of importance to existing methods of selection based upon school records and interview. To rely upon them alone or principally would be "fantastically silly." The association between test and examination success was even lower for the second than for the first M.B. There might be a number of reasons for this, but it was difficult to avoid the conclusion that test results might become of smaller and smaller significance the longer the time that had elapsed since they were achieved.

There was, Sir Frederic Bartlett added, one possible exception to this generally unpromising story. There were always a few candidates—less than 5% in this country—who for a variety of reasons slip through the meshes of the net of school record and interview and proceed to a career of almost unrelieved failure. The figures obtained in this investigation showed a critical point of intelligence-test score below which a candidate was exceedingly unlikely to pass the first examination, and in no such case, out of some 600 candidates already followed up, had the second medical examination been passed. Whether for this small minority—already indicated by other means, but not quite decisively—it was worth bringing in some existing procedure of testing was a practical question which must be decided by the relevant controlling medical authority in each country. Sir Frederic Bartlett's opinion was that it was worth while. Neither the organization nor the cost involved would amount to much, and a good deal of frustration and discontent on both sides might be avoided. The story was still incomplete. The results of the "finals" had still to come along, and it was possible that the tests would prove of greater predictive value at that stage, though Sir Frederic Bartlett thought this unlikely for two main reasons. In the first place, there was evidence that test performances became less indicative of contemporary capacity with lapse of time, and, secondly, in this country at any rate, the distribution of successes in medical finals was so widely different from that in any known intelligence test that considerable agreement between the two was nearly impossible.

AUSTRALIA'S HEALTH SERVICE

Health matters were a major issue in the 1949 Australian election, which brought the Liberal and Country Party Government into power. The Health Act of the preceding Labour Government had been strongly opposed by the medical profession and received its death blow from a decision of the Australian High Court, which ruled that part of it was unconstitutional. The present Government in four years has introduced various health measures under regulations. It now proposes to consolidate these in a Bill to be introduced in the coming session of the Federal Parliament. The Minister of Health of Australia, Sir Earle Page, has described the proposed health service to the General Assembly of the World Medical Association at The Hague this week. His address is summarized in the opening pages of the *Supplement*.

Apart from public health, and measures for the medical care of the poor which any society would accept as a charge on the community, Australia has taken the bold step of pinning its faith to the voluntary principle. The Australians are a vigorous people and might be expected not slavishly to copy the health schemes of other countries. They believe that the voluntary method is the right one for them and that it brings out the best qualities of their people. Their scheme has been based on sound foundations: the agreement and co-operation of the medical profession were secured before it was introduced; and it was introduced in stages and not placed in final form on the Statute Book until considerable experience had been obtained. The progress of the scheme will be watched with interest all over the world.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE ANXIETY STATE

BY

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An anxiety state is nature's way of announcing that life—the common life of mind and body—is disturbed and uneasy. Patient and doctor alike might welcome more precise, more self-evident indications of conflict and discord. The patient may have nothing to show for his illness—how willingly would he change it for a broken leg—and the doctor, having tried everything, may grow impatient. Nevertheless, we have in the anxiety state an authentic illness which creates a vast amount of unhappiness and incompetence.

The medical student seldom receives sufficient instruction about the psychoneurotic patient, and those seen in hospital are often atypical, with inadequate personalities. The physician brushes them aside impatiently or jokes about them. The phrase "Only nerves" suggests that "nerves" is a well-known and at the same time a discreditable complaint, best disregarded, and this is supported by the tags "A flight into illness," "Escapism," etc., which pass from one textbook to another. The student—immature and unaware of the complexities of emotional experience—with no further guidance from his teachers is unable to overcome acquired prejudice. It may be years before he outgrows his cynicism and appreciates the plain fact that reasonable, respected, and successful people are liable to neurosis. Thus he is apt to suspect an obscure physical complaint when he is consulted by a successful business man who complains of giddiness or palpitations. The young doctor learns late that intellectual brilliance and great organizing ability do not give protection against morbid anxiety. Unaware of this, he leads his patient into paths of expensive investigation, useless treatment, and probably into invalidism.

The Attitude of the Doctor

The purpose of this article is to describe the features of the anxiety state and to suggest how it may be handled by the doctor who has no special training in psychiatry, and in particular the lines along which the interview can be conducted.

Each doctor inevitably displays his own attitude of mind towards neurosis and so towards the anxiety state which is the commonest form of neurosis. But the attitude adopted is significant, since it affects the capacity to recognize the complaint. Recognition has two aspects: the knowledge of the characteristics of the condition; and, secondly, an acceptance of the fact that the anxiety state is in itself an illness and entitled to care and attention.

The sick mind, like the sick body, should be helped by considered rather than by casual methods. The doctor in general practice has not the time (and few have the experience) to use formal psychotherapy, but he can acquaint himself with the general conclusions reached by others about the neuroses. Patients should not be referred to a psychiatric clinic or to see a specialist at the first sign of trouble. The majority need never be, provided the practitioner knows how to interview patients with symptoms of neurosis. Technique is of less importance here than in any other branch of medicine. Personal consideration and a friendly approach can make the examination of therapeutic value, for in the relation between patient and doctor lie the essentials of cure or improvement.

Those people who are by nature mentally dull and therefore unable to compete on equal terms in the world are liable to contract the anxiety state. They are much benefited by our support and encouragement and by the simple prescriptions we may provide. Most sufferers with anxiety states, however, are of good intelligence, and they can be given considerable help by the family doctor who recognizes that, though sick, they are reasonable. The understanding of their puzzling illness may well be a first step towards helping them to resume responsibility for their lives. The doctor who stubbornly relies on mere common sense comprehends the anxiety state with difficulty. An unknown factor is ever present in the clinical picture—namely, the unconscious motives and the hidden mental conflict. The patient may be told of this so that he will cease to blame his environment or the shortcomings of his family. Every branch of medicine has its unknown aspects, but medical aid is not therefore withheld.

Features of the Anxiety State

Emotion plays the leading part in every anxiety state and emotion inevitably has its physical counterparts. Accordingly we always get a combination of psychological and somatic elements, although the prominence of one symptom—such as persistent pain—may distort the picture.

The somatic features, usually mentioned first, resemble closely the physical accompaniments of fear: palpitations, flushing, sweating, increased blood pressure and pulse rate, pain, giddiness, tremors, diarrhoea, polyuria. When the anxiety is protracted, headaches, nausea, and other digestive troubles, vaginismus, impotence, and lassitude may be prominent. Blundering jerky movements and restless foot movements may indicate muscular tension due to morbid anxiety. Usually one or two of these symptoms will be to the fore and fluctuations are common. The psychological symptoms include lack of concentration, unreliability of memory, apprehension, and feelings of unreality or of unreality in the external world and, as a consequence, a dread of insanity.

The anxiety may be centred on specific situations. This may become evident when we ask about travelling; whether the patient dislikes going to theatres or crossing the street; whether he has any particular fears, such as a fear of knives, of blood, of poison or diseases—for example, syphilis, cancer. Such morbid fears are usually called phobias. They are often given special labels such as *claustrophobia* and *agarophobia*, implying wrongly that they have an origin different from other forms of morbid anxiety. The purpose of the phobia is protective, and the situation or eventuality on which it is focused is shunned. If the patient cannot side-step the dreaded situation he is thrown into a panic.

The patient is often in dread of a situation where he is called on to make a direct response. For instance, should he have to drink a cup of tea his hand shakes—a distressing symptom. Again, he is unduly alarmed at being shut in a lift or a railway carriage from which there is no immediate escape. The dread of going out alone, travelling alone, and many similar situations illustrates the subtlety with which an unconscious, unknown problem is projected upon the environment.

The anxiety-ridden patient feels that many of his symptoms are unreasonable and out of proportion to the circumstances. He agrees with his doctor who reassuringly tells him that there is nothing to worry about. But his symptoms are not the result of forethought and are impervious to

logic. Such symptoms, however—palpitations, pain, etc.—alarm the patient, and his demand for medicine seems to him eminently sensible.

Morbid anxiety has a retarding effect on thought and action, and this helps us to distinguish it from normal anxiety—that is, anxiety which spurs us to fitting effort and achievement, as when the student, anxious about his examinations, works harder. Yet morbid anxiety is reasonable, although the reason is hidden, unconscious.

The Interview

The busy practitioner shudders when a patient says, "I'd better start at the beginning, Doctor." He foresees an egotistical and wandering monologue, and so cuts the interview short. The embarrassment and futility of such interviews can be overcome if we make it a rule to examine the minds as well as the bodies of those patients whose symptoms suggest "nerves." A sympathetic relationship, which is at the same time one of detachment, must be established. Without it there can be no appreciation of the patient as a person. The quality and the value of the interview depend on the personality of the doctor, his sincerity, and his capacity for understanding. Having ascertained the reason for the visit and the immediate circumstances—age, marriage, business, general health—a brief chronological survey of the patient's development, noting the personal and family history, school career, and employment record, should be obtained. In a few minutes it is possible to judge how the patient has met the customary demands of life.

We turn next to the present illness and inquire in particular about its onset, duration, course, and response to previous treatment. The emotional climate in which an illness begins is invariably important.

Previous ill-health should be noted and resemblances to the present illness. Special attention should be given to illness of a like kind in a member of the patient's family. His father may have died of cancer; his mother may have had headaches, indigestion, and a "dicky heart." The danger of psychological infection is considerable.

A fear of insanity haunts some patients and they are relieved when the subject is mentioned. They want to know if their illness is "mental." Reassurance should be deferred until the examination is finished, when it can be given with conviction—provided there is no evidence of psychosis. Similarly, the subject of suicide should be raised with the depressed patient, particularly if there is early morning waking and self-depreciation. Such inquiry will not influence the patient towards suicide, nor will he be deflected from it by the (untrue) remark that those who speak of committing suicide do not do so. Nearly all depressed patients have suicidal thoughts; and, in face of the responsibility which the family doctor is called on to bear in the management of a suicidal patient, he is justified if he calls in a specialist.

"How has the illness changed you? Were you a different sort of person previously?" Inquiries of this type are often productive. The doctor's own attitude to the conduct of life will be fully evident by the tone of his questions. If this rings true, the patient will speak freely on any subject.

The physical examination, an essential part of the investigation, is best made when rapport has been established, rather than at the beginning of the interview. The relevance of the state of mind to that of the body becomes evident when seen against the background of personal development and social adaptation.

During the examination the intelligent patient should be given some explanation of his illness: that emotion always affects the functioning of the body and this may become pronounced at times (for example, blushing, tachycardia, polyuria), and that the symptoms are not "diseases" but upset and disturbed normal processes. The patient with palpitations may think he has heart disease. Perhaps he has been told that he has high blood pressure or that his heart, although sound, is not quite healthy. Behind the fear of going out alone may be the fear of falling down dead. Most laymen believe that life hangs by a thread if there is anything whatever the matter with the heart. The patient with abdominal pain may think he has cancer, but is afraid to ask lest his fear be confirmed. Doctors are often too reticent, too cautious, and even disposed towards a bad prognosis. Optimism is usually more justified than—to the patient—ominous silence. Notice the relief of the patient on hearing: "Your heart is sound, anyhow"; "There is no growth, no sign of cancer." Organic disease may be accompanied by an ill-defined feeling of anxiety arising probably from reduced efficiency, so the physical examination should be thorough. But with the anxious patient it should not be repeated without good reason. Disordered emotions, rather than organic disease, are far more likely to be present, and the danger of treating an anxiety state as an organic illness is considerable.

The number of intellectually dull persons in the community is high, and they often contract anxiety states or other neuroses. Failure to pass routine school examinations and frequent changes of work suggest intellectual and social defect. The doctor will often get a shock if he asks a few simple questions in mental arithmetic or in general knowledge. (A smartly dressed girl of 16 insisted that there were 20 half-crowns in 30 shillings.)

Too much should not be expected from explanation and reassurance. The friendly and genuinely interested doctor increases the patient's self-respect when he listens to him, explains modestly, and gives reassurance only after careful examination. But the anxiety state may well need special treatment, and this should not be withheld in favour of sending the patient for a "complete rest"—a form of management with little to commend it.

Hypnotics and sedatives, as supplementary aids, are valuable. But when given again and again, without any effort at enlightenment, the patient is encouraged to accept "nerves" as a permanent disability. When the patient has some insight into the nature of his illness the sedative is given as a temporary measure to allay tension and not as a "nerve tonic."

Patients may mention the housing shortage and financial and business worries as "getting them down." While these are important, they are usually secondary to the patient's relation to his family and others, which if not central is again and again a crucial matter in the anxiety state. The tiresome elder sister, the alcoholic parent, the unhappy marriage, may be linked with the illness although the patient has not observed any association. The doctor should not attempt to sort out family troubles, but his patient will be helped by speaking of them and helped far more than by a tonic and advice not to worry.

An interview conducted on these lines will take perhaps half an hour. But it results in a clear picture of the patient as a whole, and in the long run time will be saved. A patient can get lasting benefit even in one interview, particularly in the early stages of the illness, provided he is given some element of insight into his illness. During the interview the doctor should bear in mind the importance of an affirmative diagnosis in the anxiety state—that is, a diagnosis which rests upon the presence of morbid anxiety. A diagnosis of "functional" or "nerves" reached by the exclusion of organic disease is of little value, as it gives no information about the nature of the illness or the person who is ill.

Relatives quite reasonably ask about their demeanour to the patient: should he be "made to do things" or "given-in to"? The cue here—and the same holds for every medical interview—is that the patient should be accepted as being ill and thus entitled to help and encouragement. The patient will lose courage if bombarded by good advice and allusions to will-power.

Psychiatric illness is seldom clear-cut, and so the interview is designed on general lines and is suitable for a wide range of patients. It is well to cast the net wide, for apparent irrelevancies often turn out to be important.

FIRST WORLD CONFERENCE ON MEDICAL EDUCATION

PROCEEDINGS OF SECTIONS

The Conference continued to meet in four Sections, which held simultaneous meetings on August 26, 27, and 28. Their proceedings are reported below in continuation of the reports in last week's Journal (pp. 486–9)

SECTION A: REQUIREMENTS FOR ENTRY INTO MEDICAL SCHOOLS

Wednesday, August 26

Section A, presided over by Dr. DONALD G. ANDERSON, continued its discussion on the general theme of the requirements for entry into medical schools.

Teaching the History of Science

Professor A. PAZZINI (University of Rome) insisted that the teaching of the history of science was not a question of the assimilation of names and dates, but rather of enabling the student to understand the evolution of science, the development of ideas, and the creation of a scientific consciousness. He was followed by Professor M. MOUQUIN (University of Paris), who stressed the value of films and museum panels.

Dr. MOGENS PIHL (Denmark) rejected compulsory teaching of the history of science and favoured an historical study of specialized subjects rather than a general course. Professor L. JUSTIN-BESANÇON (France) thought that films on historical subjects should be televised. Dr. MORRIS FISHBEIN (University of Illinois, U.S.A.) said the history of medicine must be written in the biographies of great doctors, and wanted the development of ethics and medical law taught as separate disciplines. Professor F. A. SONDERVORST (Louvain) reported that the Belgian Committee for the History of Science had invited the Government to set up chairs in the history of medicine in all four universities. Dr. M. M. WEAVER (University of British Columbia) considered that the incoming medical student benefited by a prescribed course in the history of medicine. Dr. ST. GEORGE B. DELISLE GRAY (United Kingdom) and Professor JOHN P. HUBBARD (University of Pennsylvania) also spoke.

Teaching Scientific Methods

Professor GUSTAV NYLIN (Stockholm) pointed out that it was inconceivable that the undergraduate student could be given a comprehensive knowledge in each branch of his studies. The introduction of an additional subject, "Scientific Methods," would, in his opinion, be inexpedient. But it would be productive and practical to allow time in each branch of medical education to give striking and inspiring examples of the manner in which scientific methods had evolved. Professor H. SCHULTEN (West Germany) also spoke on this subject.

The Value of Mathematics

Professor P. BONNEVIE (University of Copenhagen), in speaking under the title "Science is Measurement," said that this had been explained by the Programme Committee as covering the problem of including some mathematics in the premedical period so as to prepare the student for his introduction to medical statistics at a later period. But the subject had another meaning—the use of mathematics as a tool for all natural and social sciences, by reducing observations to figures and attempting to record experiences in terms of quantitative laws.

Miss DIANA DYASON (Lecturer in the History and Methods of Science, University of Melbourne) then described her experimental premedical course.

Thursday, August 27

Biology a Fundamental Study

On Thursday morning the place of biology, physics, and chemistry in medical education was discussed, with Dr. EDWARD L. TURNER (Washington) in the chair.

Professor JEANE VERNE (University of Paris), speaking on the role of biology in student training, described how the teaching of this subject was carried out in France. At present the premedical year closed with an examination. Owing to the great numbers seeking to enter the medical profession it had been proposed that in the large schools the examination should be replaced by a competition. But such a competition might well favour students with superficial knowledge and work to the disadvantage of others who had in them the makings of an excellent doctor.

Professor W. BARGMANN (University of Kiel) did not favour the teaching of biology to medical students only, as proposed in Germany. Before entering the university, pupils must be acquainted with the world of organisms. It was the task of the schools to provide basic knowledge of biology.

Miss M. L. JOHNSON (University College) doubted whether biology, as usually taught, really developed the powers of observation. Students saw things which they thought were there, and failed to see things which they thought ought not to be there.

How Much Physics and Chemistry?

Dr. H. C. BURGER (University of Utrecht) outlined the course of medical physics which was given at his university. Fifty lectures were given in the first year, and practical work was done on 16 afternoons. The teacher in medical physics must also be a research worker in close relation with the medical world.

Professor E. C. DODDS (University of London) said it was obvious that the whole of the teaching of chemistry should be aimed at an understanding of the structure and properties of those substances which occurred in the body and took part in metabolic processes. It was upon this field that chemical education should be concentrated. It was also necessary to study the chemical structure of drugs.

Mr. J. B. JEPSON (University of London) defined the aim as being enough chemistry to enable practitioners to appreciate advances in medical science. Dr. C. D. LEAKE wanted more chemistry.

Dr. W. E. S. MERRETT (Principal, Kano Medical School, Nigeria) said that as a physiologist he wanted students to know the hydrodynamics of the movement of fluids through tubes, but such things came only in advanced courses of physics and chemistry. One answer was to teach these subjects, but with a special medical bias.

Dr. A. S. M. NAYAR (Madras) and Dr. M. TALAAT (Egypt) also spoke.

Introduction to the Social Sciences

Professor T. S. SIMEY (University of Liverpool) said that the social sciences amplified the natural sciences and showed the student the way in which scientific method could be applied to the study of persons. He hoped that the social sciences would develop in the medical course as a simple means of enabling the student to understand those aspects of human nature which were important to the medical practitioner in his work.

Selection of Students

Dr. A. E. SEVERINGHAUS (Columbia University, New York), in a paper read by Dr. ALAN VALENTINE, stated that in the United States no group of applicants for entry to a profession were more carefully screened than those who wished to enter the medical schools. In 1952 there were 16,760 applicants for 7,425 places.

"I look for a quality which, for want of a better term, I call 'warmth,' but I feel wholly unequal to the task of trying to tell you how I arrive at a decision in this matter."

Dealing with the interview as a method of selection, Dr. Severinghaus said that at his school about one-quarter of the applicants were interviewed, and no student was admitted without an interview. However, an experienced interviewer was necessary.

Professor S. SUNDERLAND (University of Melbourne) said that there was a need for more well-trained doctors; at the same time suitably qualified students were presenting themselves in ever-increasing numbers. It seemed odd that the reaction to such a situation should be to embark on a policy of selection for entry into medical schools. The stage had now been reached where students were being coached for interviews. Interviews were not used at any subsequent stage of the student's career, and it was therefore unfair to emphasize them when he was applying for entry to the course. Melbourne University had decided to base selection solely on examination results at the end of the first premedical year. It resulted in overcrowding, but it gave all prospective medical students a chance to compete under substantially the same conditions.

Professor W. W. GREULICH (Stanford University, San Francisco), a member of an admission committee, said he had been impressed by the number of times the estimate of a candidate by equally critical, equally qualified people had differed. Dr. W. G. SMILLIE (Cornell University) and Dr. S. G. VENGSARKAR (India) also spoke.

Dr. DENIS BRINTON (St. Mary's Hospital, London) described the selection of students in the United Kingdom. The procedure was divided into three stages: perusal of application form and confidential report; the interview; and the student's first year in the school. Not a few psychologists had been critical of the value of the interview, because the test was incapable of standardization and control. But as yet there was no scientific means of measuring personality. Experience had shown that a student who failed the premedical examination seldom avoided worse trouble later.

Student Selection in India

Professor S. S. MISRA (Lucknow University) said that there were now in India 29 undergraduate medical colleges, as compared with 16 in the undivided India of 1947. About 2,000 undergraduate students were admitted every year for a five-year undergraduate course. Not more than between 30 and 40% of these students qualified in the minimum period. There were about 50,000 qualified doctors in the country, with its population of 350 millions—a ratio of 1 in 7,000. Even with the increased number of medical colleges and admissions it was not expected that there would be more than 2,000 newly qualified medical men each year—a totally inadequate number. Student selection was based on an assessment of previous scholastic achievement, and an additional premedical test. The low admission age (17), the lack of insistence on a more liberal education, and the absence of an aptitude test were responsible for the admission of many unsuitable students.

Dr. T. B. DAVIE described observations being made at the University of Capetown. Professor M. TALAAT (Alexandria University, Egypt) noted the importance of selection of teachers. Dr. DAG KNUTSON (Stockholm), Dr. MUSA GHANTUS (Lebanon), and Dr. ST. GEORGE B. DELISLE GRAY continued the discussion.

Describing student selection in Canada, Dr. M. M. WEAVER (University of British Columbia) said that medical schools in Canada were reluctant, or refused completely, to accept into the final four years in medicine anyone younger than 19 or older than 30. Lack of emotional stability or some other personality disorder might be a determining factor in the rejection of a borderline applicant. Other factors which it had been found helpful to discuss with borderline applicants included health and physical adequacy for the medical course, reading habits, the applicant's reason for wishing to become a doctor, and what he intended to do after qualification.

Dr. M. D. PENAS (University of Santo Tomas, Manilla, Philippines) and Dr. MARCEL POUMAILLOUX (Paris) also spoke.

Friday, August 28

Intelligence and Aptitude Tests

In the final session, Sir FREDERIC BARTLETT, former professor of experimental psychology at Cambridge, opened a discussion on the value of intelligence and aptitude tests. He considered that an attempt ought to be made to find a form of tests in which the "answer" must exhibit not only a final issue but also the steps by which it was approached and eventually achieved. Sir Frederic gave the first public statement on the results so far achieved in the Medical Research Council's long-term investigation of the selection of medical students. He confined himself to that part of the investigation which was concerned specifically with the use of tests. The tests used were AH5, a Cambridge high-level intelligence test widely standardized on students of university type; a group of pattern-perception tests; and the well-known N.I.I.P. Group Test 33. The correlations between test performances and examination results lay between 0.2 and 0.4 for the first M.B. (the higher figure representing only a very small part of the total population); and between −0.1 and 0.3 for the second M.B. To rely on such tests alone, or principally, would be fantastically silly—unless, of course, there was something wrong with the examination. There might be many reasons for the association between test and examination success being even lower for the second M.B. than for the first M.B., but it was difficult to avoid the conclusion that test results might become of smaller and smaller significance the longer the time that elapsed since they were achieved. The view that tests of this kind revealed stable, relatively unalterable, human properties was almost certainly wrong. Once a doctor got into the world it did not seem as if it was intelligence which counted for a great deal, but personality. Ability tests, however, might be useful if applied at a late stage of training, not compulsorily but for guidance.

Professor E. ASK-UPMARK (University of Upsala, Sweden) reported that in Sweden they had found a definite correlation between the record of a student in anatomy and his record in the clinical years.

Professor G. PATRICK MEREDITH (University of Leeds) said that university examinations did not depend entirely on intelligence. They depended a great deal on hard work and character.

Dr. H. E. THELANDER (University of California) had found that tests which tested a person under stress were the ones most likely to correlate with performance. Others speaking in the discussion were Dr. J. VAN LENNEP (Belgium) and Professor W. M. MILLAR (University of Aberdeen).

The Method and Value of the Interview

Dr. S. G. VENGSARKAR (Topiwala National Medical College, India), considering the method and value of the interview, defined the purpose of an interview as being to provide the applicant with an opportunity to display his personal qualities. The candidate should be given every opportunity to present himself favourably.

Professor GORDON KING (Hong Kong) compared the results of two "selected" years of students with two "unselected" years of students at Hong Kong, the former students being admitted after interview, the latter only on the results of the matriculation examination. The 1946 (unselected) group of students was an older group whose determination to study medicine had remained alive through five years of war, and a high proportion survived to sit the final examination. In the remaining three years (selected and unselected) little difference was noticed. Further, over 70% of students in the lowest gradings, according to interview, and only 20% of those in the highest, survived to sit for the final examinations.

Dr. T. A. DIVINE (Leeds University) commented that one could find from a personal interview the appearance of a candidate and his background, and assess his motive. Dr. E. R. BOLAND (Guy's Hospital Medical School) agreed that personal judgments could be fallacious but believed more accurate than inaccurate ones were made. He would rather

select a wife after a 20-minute interview than on the results of a competitive examination. Dr. JOHN B. LAGEN, also supporting the interview, said that when selection at the University of California was based entirely on marks there was a total "mortality" of 20–25%. During the last seven or eight years, with a selection interview, the mortality had been 7 or 8%. Professor W. M. MILLAR (University of Aberdeen) said an interview afforded the student the opportunity of making a good human relationship with some members of the faculty at the outset of his career.

SECTION B: AIMS AND CONTENT OF THE CURRICULUM

Wednesday, August 26

Section B, with Sir A. L. MUDALIAR in the chair, continued its discussion on the aims and content of the curriculum.

The Doctor is Human

Professor W. MELVILLE ARNOTT (Birmingham) said that it was sometimes suggested, mainly, he suspected, by those who because of poor education or intellectual indolence had fallen behind, that the scientific element in medical practice was in some way antagonistic to human kindliness. This was a mischievous slander which carried little weight among intelligent people. It was just as much a crime against science as against humanity for a doctor to fail in human kindliness or in sympathy. The doctor must realize that even though he could do little or nothing to stay the course of an illness his very presence gave comfort and support to the patient and the relatives. All these and many other less tangible elements in good doctoring could not be taught as formal items in the syllabus, but they could be inculcated by example.

Professor W. LÖFFLER (Switzerland) was inclined to the view that one of the chief troubles in medical teaching was that some people overestimated the practical side and others the theoretical side; it seemed advisable to synthesize the two. Any educational system must also be in accord with the mentality of the country concerned.

Dr. S. C. SEN (India) thought the time had come when medical ethics should form a very important part of the medical curriculum.

Mr. A. B. GILMOUR (Hon. Secretary of the British Medical Students Association) said that general practice was the one branch of medicine of which students knew nothing until they were qualified. They would like to have a greater knowledge of the atmosphere of general practice and all its difficulties.

Other speakers were Dr. E. ASK-UPMARK (Sweden), Dr. JOSE A. BUSTAMANTE (Cuba), Professor LEON GERIN-LAJOIE (Canada), Dr. DAG KNUTSON (Sweden), Dr. J. A. PRIDHAM (U.K.), and Dr. J. L. TROUPIN (U.S.A.).

The Introductory Clinical Course

Professor L. JUSTIN-BESANÇON (University of Paris) spoke on the introductory clinical course, in particular the influence exercised on the preliminary instruction by a knowledge of the nature of the practice which the student would follow after qualification. Must the young doctor whose career might be spent in clinical practice in a village or small town be required to undergo the full round of training in laboratory work, microbiology, radiology, and so forth? He urged that the conception of medical instruction must allow for differences, alike in method and in purpose.

Sir LIONEL WHITBY (Cambridge) spoke of the fundamental need to stimulate and encourage students' powers of observation. A student's introduction to clinical medicine in the wards should not begin with his learning the names of diseases, but with his learning how to express what he had seen, felt, or heard. Complete familiarity with the normal led quite naturally to an extremely quick observation of the abnormal.

Dr. A. C. DORNHORST (U.K.), Professor FELIX HURTADO (Cuba), Dr. DAG KNUTSON (Sweden), Dr. J. G. ORCOYEN (Spain), and Dr. M. PRYWES (Israel) also contributed to the discussion.

Teaching of Psychological Medicine

Professor D. EWEN CAMERON (McGill University) said that the teaching of psychological medicine in the undergraduate curriculum could not be exclusively concerned with hysteria and mental deficiency, with schizophrenia and manic-depressive psychoses. They would entirely fail to rise to the challenge of the times to produce physicians fit to lead the great enterprises of modern health if they so limited themselves.

Professor A. MILLAN (Mexico) emphasized the need for students to understand the mind as well as the body of patients. A patient seeking a physician's aid was not merely an animal whose symptoms could be linked with a disease.

Professor A. LAMACHE (Rennes) considered it absolutely necessary that those who studied the body should study also the psychological mechanisms which were constantly in operation; while Professor D. DE SOUZA (Brazil) thought that the emphasis should be on the student and not the patient, the first essential being that the student should know and understand himself in order to have an adequate appreciation of a patient's emotions.

Other contributors to the discussion included Dr. JOSE A. BUSTAMANTE (CUBA), Dr. OLIVER COPE (U.S.A.), Dr. M. ISELIN (France), and Dr. CHAUNCEY D. LEAKE (U.S.A.).

Thursday, August 27

Medicine and Surgery as One Discipline

On Thursday morning Dr. OLIVER COPE (Harvard) discussed the teaching of medicine and surgery as one discipline. He considered that much might be gained if the departments of medicine and surgery were willing to combine in the teaching of undergraduate medicine. A number of diseases, such as those of the gastro-intestinal tract and the endocrine organs, were traditionally taught by both departments. Consultation could be readily achieved, and where differences in point of view still existed combined group teaching by internees and surgeons could be arranged. The difficulties of such a situation were largely emotional.

"The internee would not be bothered with his technical-minded colleague, the surgeon. The surgeon, considered by tradition intellectually inferior by the internees, would be anxious, ready to have his feelings hurt, and therefore assertive from the start. But it is worth a try."

Professor A. ASENJO (University of Chile) agreed that the teaching of internal medicine and surgery should be carried out as one discipline, only separated into parts dedicated to treatment and to examination with very specialized techniques. This teaching should be carried out not only in hospital but in family surroundings.

Dr. J. A. MACFARLANE (Canada) said that if they were not to give consideration to the easement in some way of the medical curriculum then students were going to continue to spend more and more time going to lectures and tutorials.

Professor PATRICK KIELY (Ireland), Dr. T. SCHAFFER (South Africa), Dr. M. ISELIN (France), Dr. S. C. SEN (India), and Dr. A. P. THOMSON (Birmingham) also spoke in the discussion.

Teaching of Minor Surgery

Mr. WILLIAM GISSANE (Birmingham Accident Hospital) declared that the term "minor surgery" implied neither importance nor respectability—a bad introduction to the presentation of any subject in undergraduate teaching. Such an introduction had some other shortcomings. There was no purposeful attempt to build on the knowledge the student had already gained in the departments of physiology, anatomy, bacteriology, and pathology. "Minor surgery," as generally taught, placed too much emphasis on the operat-

ing act, the use of tools, the names of splints and patterns of bandages, and not enough upon the surgical principles behind the act and the use of the tools.

Dr. M. ISELIN (France) said that the student must be taught to know the type of surgery he could perform himself as distinct from that for which it was necessary to have recourse to surgical specialists.

Dr. ST. GEORGE B. DELISLE GRAY (U.K.) regarded minor surgery as that which could be—and should be—carried out by the general practitioner.

Professor A. SPINELLI (Rome) said that it was agreed in his country that students wasted their time in attending the performance of major operations. Further contributions to the discussion were made by Professor F. A. SONDERVORST (Louvain) and Professor L. G. TORNEL (Spain).

The Teaching of Obstetrics

Professor DUGALD BAIRD (University of Aberdeen) said that the teaching of obstetrics varied according to the organization of obstetrical services from one country to another, and according to national customs and the stage of evolution reached. In Britain, on the assumption that only a proportion of graduates, and only those who had had postgraduate experience, would practise midwifery, undergraduate training was now much more general and less technical than it used to be.

The standard of management of pregnancy and labour in the best maternity hospitals was now so high that the general practitioner must find it increasingly difficult to compete unless he had had special training or had constant practice under favourable conditions.

Mr. H. K. PACEY (New Zealand) then described obstetric trends in his country, where there were a well-organized medical service and a national maternity service that had operated with great smoothness since 1940.

Dr. F. M. ROSE (U.K.) was of opinion that in the teaching of the medical student the dangers inherent in pregnancy and parturition were sometimes overstressed. This country was maintaining a very expensive hospital service, and maternity beds were sometimes needlessly filled with cases which could quite well be confined at home.

Dr. MARY ESSLEMONT (Medical Women's Federation) suggested that, as they were so few, all the maternity patients in teaching hospitals should be reserved for the medical students; it was possible to arrange for patients in non-teaching hospitals to be available for midwives.

Other speakers on this subject were Dr. ST. GEORGE B. DELISLE GRAY (U.K.), Dr. G. MOUTHON (France), and Dr. J. G. ORCOYEN (Spain).

The Teaching of Paediatrics

Professor ALAN MONCRIEFF (University of London) raised the question, "Is paediatrics a branch of medicine?" In general terms paediatrics was medicine at a special age period. Usually it came into the second year of clinical studies, after a basic period of six months had been spent in internal medicine and a similar period in surgery. The General Medical Council would like to see midwifery also precede paediatrics. Clearly work on the newborn baby must be concurrent with midwifery, and this was a useful introduction to child health. It would appear that paediatrics should come somewhere towards the middle of the second year of clinical studies, after general medicine, surgery, and obstetrics, but before the specialties. With regard to the new compulsory year, a paediatric post might be suitable in the second half of this year, but not for the first six months.

Professor G. M. H. VEENEKLAAS (Netherlands) said that lectures should be given less frequently.

Dr. F. M. ROSE (U.K.) said that hospitals were reluctant to admit young children unless it was vitally necessary, or in cases where separation from the mother was not an important factor. Consequently, instruction in paediatrics might be enriched by teaching on material from general practice where one encountered cases not normally admitted to hospital.

The Place of the Specialties

Dr. H. G. WEISKOTTEN (Chairman of Council on World Education and Hospitals, American Medical Association) said that practice in the specialties had become so popular that from 60 to 70% of the recent graduates of medical schools of the United States of America had been undertaking intensive graduate programmes and then limiting their practice to a specialty. Many were complaining that the graduates looking forward to general practice now received inadequate training in the specialties during their intern or residency period. This was particularly true with regard to their training in dermatology, which was said to be a subject they had to deal with in 15% or more of their patients. In the United States too little emphasis had been placed upon the educational value of out-patient clinics.

Dr. W. W. S. JOHNSTON (Australia) said that teachers in specialties should constantly keep in mind the necessity for a balanced view so that the subject concerned was properly related to general medicine as a whole.

Lieutenant-Colonel SANGHAM-LAL (India) thought there was a tendency nowadays for cases to be referred to specialists unnecessarily, but there was also a definite risk of patients being treated by their general practitioner for far too long before being referred to a specialist. Who was better qualified than a general physician to train students in knowing where to draw the line?

Dr. S. C. SEN (India), who said it was far more difficult to be a good general practitioner than a good specialist, felt that less importance should be given to the specialties.

Professor W. MELVILLE ARNOTT (U.K.), Professor E. HUSFELDT (Denmark), and Dr. F. M. ROSE (U.K.) also spoke.

Teaching of Tropical Medicine

Dr. L. E. NAPIER (formerly professor of tropical medicine, Calcutta) referred to the doctors who went to the war areas in 1939 and successive years and found they were ill-equipped because they had not got a sufficient grounding in tropical diseases as a result of their undergraduate training and experience in temperate climates. It was necessary in a contracting world for treatment of tropical diseases to form part of the curriculum.

Sir GEORGE MCROBERT (U.K.) emphasized the particular importance of students in temperate climates being taught the fundamentals of malaria and amoebic dysentery, and other speakers shared the view that it was necessary for students to be made familiar with general questions of tropical medicine.

The Intern Year

Sir DAVID CAMPBELL (President, General Medical Council) said that it was odd to find one of the subjects chosen for discussion at the Conference "Is an intern year necessary?" He thought that was settled. The idea of the intern year was very old. In connexion with the study of medicine at Salerno the Emperor Frederick II in 1221 decreed that no one should study medicine unless, *inter alia*, his five years' medical course had been followed by an additional year of practice under the supervision of an older practitioner. No doctor who had served an internship in a teaching hospital could fail to appreciate that he had had a vital educational experience. Among other advantages of making internship compulsory was the fact that it imposed fairly and squarely on the universities the duty of approving hospitals and posts and of keeping an eye on the nature of the training and experience to be had therein.

Dr. M. PRYWES (Israel) said that since an intern year had been made compulsory in his country the standard of medicine in hospitals there had been very substantially raised.

After the discussion on this subject the Section adjourned for the day.

Friday, August 28

The Undergraduate and General Practice

On Friday morning the first paper was one in which Professor A. L. RICHARD (University of Ottawa) introduced the subject of the undergraduate and general practice by giving a definition of the general practitioner. After listing certain requisites of knowledge and skill, he said that the general practitioner should always be able to do something for his patient, if it was only to have an insight into the probable developments of the patient's disorder. A large part of the success and usefulness of the general practitioner would depend upon the influence which he exerted upon his patients, the confidence which he infused, his power to explain, persuade, and inspire. These powers were more easily wielded by a man of general culture and education than by one who had had only training in the field of exact science.

Dr. E. A. GREGG (Chairman of Council, British Medical Association) said that there were many motives which led men and women into medical practice, but he thought there were still quite a few people who went into it with the desire of devoting themselves to the welfare of their fellow human beings, and that idea was well worth cultivating in the young student. The teaching of the family doctor should be eminently practical. Most emphasis should be laid upon his acquiring skill and ability in using his eyes and hands and in thinking while doing so. The main place in which a doctor learnt his work was not the medical school or the wards, but the out-patient department.

Dr. RICHARD SCOTT (University of Edinburgh) described a unit for teaching general practice which had been established in Edinburgh in 1948 in order to demonstrate the indivisibility of medicine and to illustrate the social aspects of health and sickness. The primary concern of this unit was not, he explained, vocational training for future general practitioners; rather, it provided an opportunity for senior students to be confronted with a patient–doctor situation which they could resolve only by integrating for themselves a great deal of what they had learnt elsewhere.

Other speakers were Dr. J. R. ELLIS (U.K.), Professor A. LÁMACHE (France), Mr. R. W. HESLOP (British Medical Students' Association), Dr. J. CASTRO-VILLAGRANA (Mexico), and Drs. ST. GEORGE B. DELISLE GRAY, A. TALBOT ROGERS, and F. M. ROSE (U.K.).

The Balanced Curriculum

Sir HENRY COHEN (University of Liverpool) said that our overcrowded and confused curricula showed that we had vacillated between whether the aim of the undergraduate curriculum was to produce a good general practitioner or to lay the foundations of a medical career whatever branch of medicine was later to be followed. Spectacular discoveries in diagnosis and treatment had made increasing specialism in their techniques inevitable. Meningitis, pneumonia, malaria, subacute bacterial endocarditis, and diphtheria, to mention only a few infections, must be portrayed to-day in patterns which were unknown 20 years ago. The use of special procedures had enabled exploration by *x* rays into practically every crevice and cavity of the human body. With so vast an increase in the corpus of medical knowledge it might well be asked how could the doctor be any longer expected on qualifying to be an efficient practitioner of medicine, surgery, and midwifery. The undergraduate curriculum could not embrace the whole theory and practice of medicine; it could not attempt to teach the techniques required in the practice of specialties. It must limit its aim to laying the foundations of the doctor's training. Since medical knowledge was ever expanding, the undergraduate curriculum must favour the acquisition of enduring habits of work and thought and of enthusiasm for study, so that the doctor would remain a student throughout his professional life. The growth of knowledge in both medicine and in educational methods meant that a curriculum could never be final; it was always moving to that end, but it never arrived.

Professor TOMIO OGATA (Japan) said that if medical students were taught only what was essential, fundamental, and necessary for their future activities, and nothing more, they would not feel satisfied. They should be informed—not necessarily taught—about certain phases of actual progress in medical science.

Dr. JOHN BURTON (U.K.) said that *doctor* meant *teacher*, and one of the sources of imbalance in most curricula was the fact that the student was regarded as an empty vessel into which knowledge had to be poured, and never as the doctor who had got to be the teacher of the future.

Professor PATRICK KIELY (Ireland) asked if they were not overemphasizing the itinerary which the student should carry in his pocket as against the ideology which he should have in his mind.

Dr. J. G. ORCOYEN (Spain) and Dr. L. BINBAKYA BIDYABHED (Thailand) also spoke in the discussion.

SECTION C: TECHNIQUES AND METHODS OF MEDICAL EDUCATION

Wednesday, August 26

The general theme in Section C was the techniques and methods of medical education. The Wednesday morning session was devoted to medical illustration, and many examples were shown of visual aids, the cinematograph film, and the still picture. Professor A. GARRETON-SILVA (Chile) presided over this session.

Visual Aids in Education

Dr. P. N. CARDEW (St. Mary's Hospital) said that visual methods of education had in the past proved a controversial subject, especially when applied at university level of study. There had been a feeling that while they might be suitable for schoolchildren the written or spoken word was more dignified and appropriate for a learned profession. Yet many newly qualified doctors remembered the symptoms of a disease by visualizing a certain page of their favourite textbook. The visual memory was receptive and tenacious but could as easily be confused by poor illustration as stimulated by the expert use of visual symbols. Dr. Cardew described the varied uses to which lantern slides, still pictures, and motion pictures could be put.

Dr. KENNETH SODDY (World Federation for Mental Health) discussed the uses of the one-way observation screen. Its main value clinically was in the observation of the behaviour of young children, but, with the patient's consent, it had obvious uses in the field of psychological medicine.

The Moving Picture in Medical Education

Mr. RALPH P. CREER (American Medical Association) said that educational psychologists were of opinion that the rate of learning was based on experience; therefore one of the most effective methods of teaching was to provide direct experience or an adequate substitute. That was where the use of the motion picture came in, for many types of previously unobtainable experiences were now only as far away as the motion picture projector.

But, like other aids to teaching, motion pictures had their limitations. They placed a new responsibility on the teacher, for they involved special preparation and a new method of teaching.

The Still Picture

Professor TOM JONES (University of Illinois) discussed the group of visual teaching media referred to as still pictures. These included all forms of inanimate pictorial representations, from simple blackboard diagrams to full colour photographs and drawings. Still pictures were more widely used to-day in medical schools than either motion

pictures or three-dimensional material. It would be difficult to imagine anatomy, pathology, and surgery being effectively communicated without photographs and drawings.

Tracing the history of medical illustration, Professor Jones said that probably no single event had contributed so much to the advancement of medical knowledge as the basic discovery of photography with all that it implied. With the necessity of crowding into a curriculum all the material now considered necessary for the training of a physician or surgeon, newer methods of teaching had to be found. Language must always be the main stream of communication, but, to quote a report on the use of audio-visual aids in the U.S. Armed Services: "The concepts of more learning in less time, of greater retention, and of more realistic instruction have reinforced the contention that learning can be facilitated and made more meaningful through appeal to all the senses."

Among those who took part in the discussion or made comments on the examples shown were Professor G. P. MEREDITH, Professor ROBERT CRUICKSHANK, Mr. C. E. ENGEL, Dr. PATRICK COLLARD, Dr. PETER HANSELL, Dr. JOHN BURTON, Dr. ROBERT OLLERENSHAW, and Mr. A. B. GILMOUR, honorary secretary of the British Medical Students Association.

Thursday, August 27

The Lecture and Group Discussion

On Thursday morning, with Professor A. Hurtado in the chair, Professor G. P. MEREDITH (University of Leeds) discussed the art of lecturing and of organizing discussions. He listed three main reasons for the ineffectiveness of many lecturers: faulty delivery; the forcing of words to perform functions for which other media were more appropriate; the distribution of the lecturer's attention over too many techniques. The lecture was not the appropriate medium for the presentation of factual information. Its primary function was the communication of theoretical concepts. His impression was that in university teaching generally there were too many lectures. The effect of the lecture should be the establishment of a new concept or group of concepts in the mind of the student. On the other hand, the discussion group was adapted to exploring the implications of concepts and to answering all those questions which immediately arose in the mind when new concepts were grafted on to old knowledge.

Mr. K. H. MCALLISTER (Further Education Organizer, Somerset County Council) said that group discussions ensured a flow of ideas. With the lecture it was often the bright members of the audience who were the pacemakers, and the teacher adjusted himself to their standard.

Professor IAN AIRD said that at a recent conference in London on the application of group methods in medicine a hundred medical teachers separated themselves into four groups, each with a non-medical educationalist to guide it. The technique was a little difficult at first, but it quickly became obvious that it might have a real and practical application to clinical medicine. Dr. JOHN BURTON (Director, Central Council for Health Education) said that the group discussion method had the advantage of putting the teacher in a position of finding out what his students really knew, what were the emotional barriers to their learning, and how he could adjust his teaching to their levels and concepts. Further, in a discussion group, a teacher was examining while he taught. Dr. VICTOR SORIANO (Uruguay) said that in his school the lecture and discussion group systems were combined, and the lectures always ended with questions. Professor S. S. MISRA (University of Lucknow) said that he had found that frank confession by the teacher that he could not answer a student's question did not diminish the teacher's prestige.

The Full-time Teacher

The full-time system of appointment to the teaching staff in the Faculty of Medicine, as followed at the University of Chicago, was described by Dr. L. T. COGGESHALL, dean of the Division of Biological Sciences in that university. The physicians so appointed were free to follow their three major interests and responsibilities, namely, teaching, engaging in scientific research, and giving medical care, "without the limitations and distractions" generally imposed by private practice. The system had been successful in fulfilling the primary functions of a medical school, though the speaker admitted that such a system might not be universally applicable to the purposes of medical education.

Professor H. B. WULFF (Lund University) said that if doctors and money were available the full-time system was excellent, but it was a good thing, nevertheless, for many schools to have well-paid teachers, not full-time, but allowed a strictly limited private consulting practice.

Professor FELIX HURTADO (Cuba) said that the full-time system was inappropriate in his country because such a professor would be unduly limited in his experience of patients.

Dr. FRANK FREMONT-SMITH (New York) said that the main disadvantage of the full-time system was that it tended to isolate teachers from the realities of medical practice in the communities which surrounded their medical schools, and therefore there was a tendency for them to teach a practice which would be far removed from what most of their students encountered later in their career. Mr. D. H. PATEY (Middlesex Hospital) said that in England consultants got very good payment for the work they did under the National Health Service system, and therefore there was an opportunity for those connected with hospitals to devote their major energies to teaching and research. Professor E. HUSFELDT (Denmark) held that the university professor should have some private practice. Dr. M. POUMAILLOUX (Paris) said that a doctor who devoted the whole of his life to hospital practice and had no private practice had no normal conception of medicine as it was to-day.

The Place of the Textbook in Teaching

Professor MAURICE MULLER (University of Lille) said that the teaching of medicine could be divided into three parts: primary teaching leading to a doctorate, supplementary teaching enabling the doctor to keep his knowledge up to date, and higher education which led to hospital and university appointments. In each stage different textbooks were needed.

Professor J. E. DEBONO (University of Malta) said that he had no quarrel with textbooks in general, but he had some quarrel with *the* textbook—the book which the student considered to contain all necessary knowledge. This was a snare and a delusion. Textbooks were not meant to be read right through, but to be dipped into. Professor H. WENDEROTH (Germany) and Professor J. N. P. DAVIES (Uganda) also spoke.

Library and Reference Services

Lieutenant-Colonel FRANK B. ROGERS, director of the Armed Forces Medical Library, Washington, discussed the value of library and reference services in undergraduate medical education. He said that in the United States more than half the schools gave instruction in the use of the library and in bibliographical methods. The librarian could show the student that there were better ways of finding material than by paging aimlessly through volume after volume of likely journal titles.

Mr. C. C. BARNARD (Librarian, London School of Hygiene and Tropical Medicine) said that the library should be an integral part of a school and the librarian a member of the teaching staff. He outlined a scheme which was in operation at his school consisting of three lectures on library usage, with demonstrations on the use of the catalogue.

Professor JOHN F. FULTON (Yale) emphasized the importance of the library in medical school curriculum. Dr. F. A. SONDERVORST (University of Louvain) raised the question of the relative value of central and departmental libraries. He found that students preferred scattered local libraries, each dealing with different branches of study in the various departments of the university. Dr. H. E. MACDERMOT (Editor,

Canadian Medical Association Journal) referred to the Osler library—not a memorial library but Osler's own library—in Montreal. This was of great interest to students and other visitors, to whom it was shown by a man who knew it intimately. Professor J. N. P. DAVIES (Uganda) spoke of the need for creating in the library a pleasant atmosphere, with good lighting, comfortable chairs, and works other than medicine. The library should be open for very long periods, and located conveniently to the medical school.

The Medical Museum

Dr. C. J. HACKETT, Director of the Wellcome Museum of Medical Science in London, spoke of the role of teaching museums in undergraduate education. The contents of such museums should be broadened to include all aspects of medicine. Specimens of pathological conditions, parasites, drugs, and the like, and illustrations and diagrams should be brought together with carefully prepared summaries so that the student might see a disease as a whole, from cause to prevention. He suggested the establishment of a Medical Museums Bureau on a national or international basis for the dissemination of information on museum techniques and for originating and exchanging illustrative material and specimens.

Professor E. F. D'ATH (University of Otago, N.Z.) said that most of the teaching medical museums were in the main pathological museums, having been developed as adjuncts to the teaching of pathology. With the co-operation of other teaching departments the museum could be broadened in scope and made more attractive.

Professor M. MARTINEZ-BAEZ (Mexico), Dr. B. CASTLEMAN (Massachusetts General Hospital, Boston), Professor TOM JONES (University of Illinois), Miss SYLVIA TREADGOLD (Guy's Hospital), and Dr. LEWIS (South Africa) also joined in the discussion.

Teaching the Teacher

Dr. R. D. LAWRENCE (King's College Hospital) said that some attention had been paid in recent years to the question of the selection and training of the teacher, but there had been almost nothing done in this country to ensure that teachers of medicine could teach or to help them if they could not. Teachers of medicine were chosen on account of various qualities and achievements, but not for their teaching ability. Training in teaching did not exist. It was sometimes said that good teachers were born and not made. That was an axiom in which he did not believe. The teacher should have a ready flow of words, a capacity for logical arrangement, and an ability to keep what he taught at the student level. He must also have a character and personality which interested the students, and be able to tease them and laugh with them. Dr. Lawrence referred to the deplorable diction and delivery of many lecturers, and suggested week-end courses for teaching teachers to teach.

In the course of a brief discussion Professor IAN AIRD mentioned an experiment which was being tried out in London whereby it was proposed to give certain men exercises in lecturing and bedside teaching. Dr. F. FREMONT-SMITH (New York) said that the teacher–pupil relationship was analogous to the parent–child relationship, and must be a two-way process of communication. Dr. W. HOWARD HUGHES (United Kingdom) suggested that the schools of the future which produced the finest teachers would be those which had the best extra-curriculum activities, including sport and dramatic societies.

Friday, August 28

The Examination Paper

The final session in Section C began with a discussion on the examination paper.

Professor IAN AIRD (University of London) said that practical examinations in medicine were, to his mind, too short and hurried, and the examination paper might well be used as a sieve or filter to reduce the number of candidates presenting in the practical examinations.

"After having read many thousands of examination papers, I feel competent, not to say whether the writer of the examination paper was a good doctor, but often to say quite confidently, on the result of the written examination alone, that a candidate should not be allowed to practise medicine. If a candidate proved himself in the written examination to be in error on a number of important facts, or not to be provided with a satisfactory number of facts on a given subject, or if he proved to lack understanding of an essential pathological or therapeutic process, that candidate should, on the result of the written examination alone, be rejected, and not present himself for the other parts of the examination. This would allow a longer time than at present available for the practical, oral, and clinical examination of doubtful candidates."

Professor MUNAWAR ALI, President-elect of the Pakistan Medical Association, considered that undue importance was given to the examination paper. The insistence on 50% marks in each component of the examination to avoid failure was unsound in principle. The type of question in vogue at present should be replaced by questions that could be answered on the basis of a general knowledge of medicine gained by the students through their clinical observation and study of patients, not merely on the strength of the cramming of textbooks.

Dr. J. L. TROUPIN (World Health Organization) said that in dealing with his students at examinations he had told them that they were at liberty to bring any textbooks or notebooks they wanted, and to make any inquiries, even over the telephone. The students thought it a jest, but they invariably said that they preferred an examination where they did not have books and could use only what they had learned.

Professor BEATRICE JOLY (University of Ibadan, Nigeria) suggested that the final examination might be regarded as a useful method of evaluating teaching and teaching ability as well as student proficiency. The examination papers in any particular subject should be available to the senior members of the department, by whom they should be assessed very carefully with a view to criticizing the teaching which had contributed to the examination results.

Others who made brief comments were Dr. S. S. MISRA (India), Professor F. AKKRAWI (Bagdad), and Professor M. D. PENAS (Philippines).

Practical and Oral Tests

Professor A. GARRETON-SILVA (University of Chile) discussed methods of testing the degree of knowledge acquired by the student. Some of these methods were of a general character, common to all subjects; others were of a special character. In the preclinical period the criterion of progress was the laboratory work done by the students under the vigilance of the professor and his teaching staff. In the clinical period the best criterion was the care of a patient by the student together with the professor, but here it was essential that the student should share the responsibility for such care.

Dr. R. A. MOORE (Washington University) described a multiple-choice examination which was gaining favour in the United States. This meant putting questions to the students and suggesting a number of answers, one, or perhaps more, of which was correct, and the student was asked to say which in his view was the proper answer. The answers were graded electronically so that no error on the part of the assessor came in. He also described a method of comparing one school with another, taking a mean for all the students.

Why Students Fail

Mr. T. R. HENN, Senior Tutor, St. Catherine's College, Cambridge, in a thoughtful paper, discussed the reasons for student failure. He was inclined to think that any one or more of a number of possible "traumatic" conditions, fostered by the strain of the social and intellectual life of a university, were finally brought to a head, as it were, in a false attitude to the university, to the examination, and the final degree which the examination represented. Those of them who were concerned with the universities could do much to ensure that only intellectually suitable students were admitted, though it was seldom possible to investigate psychiatrically a likely predisposition to a breakdown, nor

would it be advisable to attempt anything of the kind. And who would dare to exclude a potential Shelley or Baudelaire? What conflicts would analysis have revealed in John Donne or Milton? What was possible was to develop in teachers and students a sane attitude to all examinations. Mr. Henn went on to speak of ways in which examinations and the preparation for them could be set in a fairer perspective.

Touching on suicides among university students, Mr. Henn said that the incidence at the older universities in this country was higher than at the younger, probably reflecting the higher standard of entry and of examination, and perhaps the different rhythm of living. Sexual disturbances were not, in his experience, an important cause of failure.

A student, Mr. A. P. OOMEN (Netherlands), said that the relation between medical students and their teachers should not be just the same as that which existed between other students and their teachers—that is to say, that the teachers gave of their wisdom and knowledge and the students just took it in. The making of good doctors was not, in the first instance, a question of absorbing knowledge, but of developing a wiser, better, and more understanding man.

Professor D. E. CAMERON (McGill University) mentioned some of the reasons why students failed. One of the reasons was the development of neurotic or even psychotic difficulties. There was the student who "blew up" in an anxiety state at examinations. What guarantee was there that he would not "blow up" later on at an operation or a delivery? There were students who showed a major change in motivation during the course of their studies, perhaps as a result of marriage and a wife who discouraged them from pursuing a medical career. Again, the woman student had a most confusing role to play. She had to compete with and act like a man, and was often prevented from participating, as her sisters could, in social life. An unusual number of problems arose in the case of the woman student.

The discussion was continued by Professor AKKRAWI (Bagdad), Professor E. ASK-UPMARK (Sweden), and Professor VICTOR SORIANO (Uruguay).

SECTION D: PREVENTIVE AND SOCIAL MEDICINE

Wednesday, August 26

In Section D, under the presidency of Professor A. STAMPAR, the discussion was continued on preventive and social medicine.

The Teaching of Epidemiology

Professor THOMAS FRANCIS (University of Michigan) opened the proceedings with a paper on the teaching of epidemiology. He suggested that epidemiology should be introduced into the curriculum as a study of pathogenesis: ideally, the teaching of epidemiology should permeate all phases of medicine which related to pathogenesis and its applications. Of one thing he was sure, that the more epidemiology was recognized as and believed by the instructors to be an integral part of medicine and medical research rather than some esoteric or merely intellectual activity the greater its effectiveness would be.

Dr. J. WICKSTRÖM (Finland) said that the importance of epidemiology was little acknowledged in practice. At none of the ten medical schools in the Scandinavian countries was there a professorship of epidemiology; lecturers were in charge of the instruction, and one could not expect an adequate competence in education where such a system prevailed.

Professor ROBERT CRUICKSHANK (St. Mary's) said that there were three main avenues along which medicine had made progress—namely, laboratory experiment, clinical signs, and the epidemiological method. Only in recent years had it been realized how applicable the epidemiological method was to a whole variety of diseases. There was some danger of mistaking applied bacteriology for fundamental principles. A great deal was taught about the modern methods which the laboratory used, but this did not constitute the teaching of epidemiology, which was essentially the pathogenesis of disease in the community. He outlined the teaching of preventive medicine at St. Mary's.

Professor P. BONNEVIE (Copenhagen) said that epidemiology was a part of hygiene, which was concerned chiefly with the environment and the action and attitude of man towards it. Dr. P. S. WOODRUFF (Adelaide) emphasized the importance of the student's participation in epidemiological studies. Professor STAMPAR did not consider that there should be special chairs in epidemiology; the subject should be included in hygiene and social medicine.

Demography and Vital Statistics

Professor AXEL STRØM (Oslo) discussed the teaching of demography and vital statistics. Seminars and colloquies were the methods best suited for teaching these subjects. Lectures were, in his opinion, less valuable.

Dr. PETER PAU (Trinidad) said that he had found an acquaintance with games of chance a useful introduction to statistics in the teaching of students. He had also enjoined his students to study crowds, as at football matches, in order to familiarize themselves with the notion of epidemic disease.

Professor STAMPAR mentioned that as an examiner he had been struck by the fact that many students were quite unable to state the population of their own town or county or the birth and death rates.

Teaching of Medical Genetics

Dr. J. A. FRASER ROBERTS (Stoke Park Colony, Bristol) contributed a paper on the teaching of medical genetics, a knowledge of which, he said, was of practical importance in learning and practising medicine. Instruction should not be postponed to postgraduate courses, and the genetics taught in connexion with biology should be supplemented by teaching on medical genetics during the clinical years. Five or six systematic lectures should suffice.

Dr. M. POUMAILLOUX (Paris) read a short contribution to the discussion sent by Professor M. LAMY, of Paris. In France, in the introductory year, during which the natural sciences were taken, twenty lectures were devoted to animal genetics, but until the recent establishment of a chair in medical genetics at Paris (of which Professor Lamy is the holder) there was no teaching in genetics from the human point of view.

Dr. J. B. JEPSON (Middlesex Hospital) emphasized the contribution which the course in chemistry given in medical schools should make to the teaching of medical genetics and of social medicine. The occurrence and importance of variation, genetical and otherwise, could be readily demonstrated as part of the course in chemistry and biochemistry, and it was here, in the first instance, that it should be emphasized as an important factor in clinical and social medicine.

Thursday, August 27

Social Psychiatry

The proceedings on Thursday began with a paper by Professor H. C. RUMKE (University of Utrecht) on the teaching of social psychiatry. Such teaching, he said, should be part of the whole teaching of medicine. Social psychiatry was not a matter only for the student who intended to be a psychiatrist or a specialist in mental health, but also for those who wished to be general practitioners. The more the general practitioner knew about social psychiatry the higher his standing would be. The speaker gave a survey of the teaching of the subject in his own university.

Dr. J. L. HALLIDAY (Department of Health for Scotland) said that there was widespread failure to appreciate the psychology of and social approach to sickness, and to understand what action of a therapeutic or preventive kind such an approach indicated. When the enormous mass of recurrent illness and chronic invalidism was realized it was evident that psycho-social medicine—a term he preferred to

"social psychiatry," which was too exclusive—needed to be incorporated in the curriculum.

Dr. PETER PAU (Trinidad) described some of the difficulties of social medicine in the West Indies, the tracing of family patterns, and the ascertainment of taboos. Professor W. G. SMILLIE (Cornell University) mentioned the useful findings obtainable through the students' health service. Illness among students was often the result of emotional stress. By enabling the student to understand himself and his fellow students he was the better equipped to understand his future patients. Dr. R. SUTHERLAND (Leeds) said that it was often difficult to elicit the underlying tensions in an interview with the patient, and here he had found a use for the tape recorder.

Social Environment and Individual Illness

Professor A. QUERIDO (University of Amsterdam) said that, notwithstanding the development of technical methods and the attention these received in teaching, the individual patient with his complaints and symptoms was the pivot of all true clinical instruction in the art and science of medicine. How could the social factors which had contributed to the illness of a patient be assessed in clinical teaching? And how could the social factors which might assist the patient's recovery be properly evaluated? It was a problem of integrating social data in the same way as the data resulting from *x*-ray or pathological investigation were integrated. But what specialist was to do this integration? Was the social worker or almoner comparable with the radiologist or pathologist? He was doubtful whether the social worker could bring the teaching up to the standards of medical education.

Professor YOSHIO KUSAMA (Keio Gijuku University, Tokyo) said that when his department in his school of medicine was organized in 1928 it was called "preventive medicine." To-day it was called "hygiene and public health." The public health discipline for undergraduate medical students in his country was not markedly different from what it was in others.

Home Setting in Medical Education

Dr. J. M. FAULKNER (Boston University School of Medicine) described a programme devised at his university which brought students into direct participation in the care of patients in their homes. The programme was organized as the home medical service, which was a division of the Department of Preventive Medicine. This service was an extension of the out-patient department of the Massachusetts Memorial Hospital. It provided medical care in the home for the indigent in a circumscribed area of Boston immediately surrounding the hospital; this was a slum district, with a population of about 50,000. Fourth-year students were assigned to the service, full time, for one month. In addition each third-year student was assigned a patient from the service whom he followed for two years. About 15,000 visits were made annually to about 5,000 patients, 85% of whom were treated at home.

Professor MARCEL GRAFFAR (University of Brussels) said that at the end of the war his university decided to set up a chair of social medicine as distinct from the chair of hygiene. Of this chair the late Professor Sand had been the first titular holder. The co-existence of the two chairs had been entirely successful, and each professor had co-operated with the other. Professor Sand had realized the need for complementing theoretical instruction by practical exercises, and since 1947 the students in their penultimate year had been sent out into the field to study social problems and to make routine reports on their observations.

Among others who took part in this discussion were Dr. JOHN PEMBERTON (University of Sheffield), Dr. E. M. DIMOCK (University College Hospital), Dr. K. NELSON (Richmond, Virginia), Dr. JULES P. DE MELLO (Nairobi), and Dr. DAG KNUTSON (Stockholm).

Professor STAMPAR said that in Zagreb the students were expected to go out in groups to the villages.

Teaching of Occupational Health

Professor A. J. LANZA (Department of Industrial Medicine, New York University Postgraduate Medical School) mentioned the difficulties which had attended efforts to introduce industrial medicine into the undergraduate curriculum. It might well be that before this was achieved the scheme of medical school education would have to be reshaped. In the meantime they kept on trying to establish their "beachhead" in the third or fourth year classes.

Dr. RICHARD SCHILLING (Nuffield Department of Occupational Health, University of Manchester) pleaded for the integration of all the specialties bearing on this subject. One of the great factors encountered in occupational health was the unwillingness of many workers to place themselves under medical care owing to their fear of being deprived of their employment. The teaching of occupational health should be an integral part, with social medicine, of all clinical teaching, and was most effectively given by clinicians.

Professor P. BONNEVIE (University of Copenhagen), Professor THOMAS FRANCIS (University of Michigan), Dr. J. J. GILLON (Medical Inspector-General of Industry in France), and the Chairman (Professor STAMPAR) took part in the discussion.

Student Health Services

Sir ALAN ROOK, senior health officer, Cambridge University, suggested some ways in which use could be made of the student health service for giving practical tuition. One way would be for the instruction of medical students in immunological procedures. Mantoux testing and B.C.G. vaccination of the students themselves, at present done by student health officers, could be used for teaching. He indicated various other ways in which the student health service could be used for the dissemination of knowledge of social and personal hygiene.

Dr. P. S. WOODRUFF described the student health services in Adelaide, and Dr. PETER PAU (Trinidad) those obtaining in the West Indies.

Infant and Child Care

Dr. MARIJ AVCIN (Yugoslavia) opened a brief debate on infant and child care as a medico-social problem.

Professor JOHN CRAIG (University of Aberdeen) said that both the teaching of social medicine and researches into social conditions were becoming more difficult because the more obvious environmental diseases in this country occurred less often. But many questions remained without an answer.

Every student should spend at least a month with a family doctor on his rounds, getting some insight into conditions in the homes of the people. Ward and out-patient work, visits to families in their homes, attendance at child welfare and aftercare clinics, were all useful teaching agencies for medico-social knowledge. Most helpful of all was the teacher himself. Each teacher should strive, therefore, to know his own region intimately, its history and geography, its climate and diseases, its culture and its social problems.

Dr. ROBERT SUTHERLAND said that health education should start with paediatrics, and Dr. MCLENNAN quoted the advice of a paediatric teacher to his students: "Never believe a word the mother says."

Friday, August 28

The Teaching of Nutrition

The first address in the closing session of the Section was by Dr. H. M. SINCLAIR (Oxford) on the teaching of nutrition. The emphasis on nutrition in the preservation of health, he said, was by no means new—witness the teaching in the school of Salerno in the twelfth century. The best method of stimulating an interest in nutrition was probably not by postgraduate study but by a year's research at the

end of the training in physiology and biochemistry. This period of research had proved very valuable at Oxford, where the degree of B.Sc. was available for it.

Mr. HARRY LILLIE (Scotland), Dr. PETER PAU (Trinidad), Dr. DAG KNUTSON (Stockholm), and Dr. ROBERT SUTHERLAND also took part in the discussion.

Housing in Relation to Health

The Section then turned to the housing question, on which there was a paper by Professor J. M. MACKINTOSH (London School of Hygiene and Tropical Medicine). Instruction to the medical student concerning housing should be given in such a way as to stir the student's interest and imagination, and should be related to health and sickness. The primary aim in teaching undergraduates about housing conditions should be to illustrate by example the ill effects, both mental and physical, of bad housing. The best approach was the historical one: the student should be shown by illustration and subsequent visiting what slums were and how they had grown and the methods by which they could be eliminated.

The discussion took the form of statements about housing conditions in several countries, particularly in the East.

Integration of Preventive and Social Medicine

The final paper was on the integration of the teaching of social medicine and preventive medicine in the curriculum. Professor J. P. HUBBARD (University of Pennsylvania) said that social medicine was not a separate discipline with a discrete body of knowledge; rather it was an attitude which permeated the entire medical curriculum. It was founded in the basic sciences and in clinical medicine; it drew also upon the social sciences, and in its application called for a health team which included not only the practising physician and the health officer but also the visiting nurse, the social worker, and many others with specialized skills.

Professor STAMPAR, from the chair of the Section, in closing the proceedings, said that he himself had learned a great deal from the many original contributions which had been given, and it was evident that social and preventive medicine was gaining ground in the education of the medical student.

CONCLUDING PLENARY SESSION AND CLOSING PROCEEDINGS

After the four Sections had finished their work the Conference assembled in plenary session on Friday afternoon and Saturday morning, August 28 and 29. Sir LIONEL WHITBY, the Conference President, was in the chair during Friday afternoon, and Professor W. MELVILLE ARNOTT, the Deputy President, presided on Saturday, when Sir Lionel Whitby had to leave for Canada. At these concluding sessions the four Sectional vice-presidents, Dr. Victor Johnson, Sir A. L. Mudaliar, Professor A. Hurtado, and Professor A. Stampar, addressed the Conference, and they were followed by the rapporteurs, Dr. Raymond Whitehead (Section A), Dr. A. Morgan Jones (Section B), Professor Ian Aird (Section C), and Dr. Charles Fletcher (Section D). Each rapporteur summarized the work of his Section and there was then a general discussion on it. Some comment on the remarks of the vice-presidents and rapporteurs is given in a leading article at p. 549, but a full report of their speeches will be given in next week's *Journal*.

During this session the President referred to the death of Dr. René Sand, who was to have presided over Section D, and the Conference stood for a few moments in silent tribute. An obituary notice is printed at p. 571.

Closing Proceedings

On the last day of the Conference, after the final discussion, Professor Melville Arnott said from the chair that there was no doubt whatsoever that the Conference had been very well worth while. He was quite sure that nobody was happy or complacent about medical education, and the Conference had caused—and would continue to cause—much earnest thinking. But he hoped it would be remembered that plans could never triumph over individuals, and that they would not be hypnotized into too much planning.

Dr. T. C. ROUTLEY, chairman of the Organizing Committee, said that Dr. E. Grey Turner, the indefatigable secretary of the Local Arrangements Committee, had informed him that the entire proceedings had been recorded on 200,000 feet of magnetic wire. But the really permanent record would be in the minds of those who had attended. It was just three years ago that Dr. Hugh Clegg brought forward the idea of this World Conference. The idea "took legs," but the "legs" had new roads to traverse and no road maps to guide them. The result, however, had more than justified the labours entailed. He acknowledged with the sincerest appreciation all who had assisted—the World Health Organization, and the collaborating bodies, the Council for International Organizations of the Medical Sciences and the International Association of Universities; the industrial corporations who had made substantial gifts; the authors of the papers; the interpreters who had rendered excellent service; the Society of Friends, in whose house most of the meetings had been held; the host organization, the British Medical Association and its officers and employees, who had given the most unselfish service; the officers of the Conference, its vice-presidents and rapporteurs, and those who had entertained the members at a succession of social events. He also expressed gratitude for the service, continuing through the years and emphasized in the present Conference, of the secretary-general, Dr. Louis Bauer, and his executive assistant, Miss M. L. Natwick, and finally for the work of Dr. Hugh Clegg, secretary of the Programme Committee, who would continue to labour in the preparation of the published proceedings.

The meeting by prolonged applause endorsed Dr. Routley's remarks, and the Conference then terminated.

SOCIAL OCCASIONS

As host organization to the First World Conference on Medical Education the British Medical Association led off the round of receptions and visits with a reception at B.M.A. House on August 22. The Great Hall was filled with a gathering of delegates from all over the world, many of them accompanied by their wives and families. The guests, who numbered nearly 500, were received by the President of the B.M.A., Mr. J. W. Tudor Thomas, and Mrs. Tudor Thomas, and by the Chairman of Council, Dr. E. A. Gregg, and Miss M. Gregg. On Sunday, August 23, there was an excursion to Cambridge, where the visitors had lunch in Trinity College and tea at Downing, where Sir Lionel and Lady Whitby were the hosts. During the week the Conference was in session receptions were given by the Government, the Royal Society of Medicine, the University of London, the London County Council, and the Ciba Foundation. There was also a sherry party at B.M.A. House given by the Medical Women's Federation to medical women from overseas. On the afternoon of August 25, when the delegates had a half-holiday, there was a river trip down the Thames to Greenwich. At the Conference Banquet on August 28, held at the Dorchester Hotel, Sir Lionel Whitby was in the chair. Sir A. L. Mudaliar gave the toast to the World Medical Association, and this was seconded by Dr. M. Poumailloux. The response was made by the secretary-general, Dr. Louis H. Bauer, who said that he believed the doctors of the world had done more to improve international relations than all the diplomats put together. Dr. Dag Knutson proposed the health of the guests, and Miss P. Hornsby Smith, Parliamentary Secretary to the Ministry of Health, replied. In congratulating the organizers she said that few conferences had commanded the substantial and responsible editorial comment which the First World Conference of Medical Education had achieved. Professor A. Hurtado proposed the toast to the president, and Sir Lionel Whitby made a brief response.

AIDS FOR THE DISABLED

[BY A SPECIAL CORRESPONDENT]

Among the attractions at the first International Congress of the World Confederation for Physical Therapy, which opens at the Central Hall, Westminster, on September 7, is an exhibition of self-help devices, splints, and gadgets for the disabled. The exhibition remains open until September 12, and it should prove of great practical value to anyone responsible for the care of disabled persons. The exhibits have come from the United States, Canada, and South Africa, as well as from many parts of Britain. It is possible to describe only a few of them here.

FIG. 1

The British Red Cross is showing several gadgets and adaptations for the home-bound cripple. The padded eating utensils and the long-handled toilet aids (Fig. 1), although already widely known, deserve special notice as they are so useful, so simple, and so highly valued by the patients who need them.

The American Physical Therapy Association is exhibiting a collection of aids selected from the many which have been developed in the United States. They include devices to help various types of cripple with the activities of daily living, such as dressing and undressing, toilet, eating, communication, getting about the house, and doing housework. A gadget seems to have been devised to overcome every rehabilitation obstacle.

FIG. 2

There are several exhibits from the Canadian Physiotherapy Association. From the Physiotherapy Department of Ottawa Civic Hospital there is a detailed description of an adaptable bed which can be tilted to 85° by a jacking system to allow a patient to put his feet to the ground and stand up without effort. The bed appears to be sturdy and easily constructed. Other exhibits are splints adapted to take attachments when there is complete loss of control of wrist and hand and an adjustable chair for cerebral palsy patients. Another chair shown by the Canadian Physiotherapy Association is most ingenious (Fig. 2). It consists of a framework on wheels with two overhead bars whose height can be raised on a ratchet. The patient is wheeled underneath the bars, from which shoulder straps are attached to large comfortable axillary pads. The patient is then wound up to standing height, in which position walking re-education can be begun, with no fear of falling.

From the Royal Victoria Infirmary, Newcastle-upon-Tyne, there is a simple device for the retraining of plantar flexion in cases of fractured calcaneus. There are some examples of Mr. Norman Capener's (Exeter) "lively" splints. Each splint is made to suit the individual problem. Its object is to allow both physiological rest and an appropriate amount of function. There is no doubt that similar splints could be more widely used. The Central Council for the Care of Cripples is showing gadgets to assist crippled housewives do their housework and manage their kitchens. Mr. H. A. Turnbull, M.C.S.P., has sent details of a crutch attachment (Fig. 3) for use by a patient who needs a crutch but cannot control one because of insufficient grip in the hand. This should prove useful in the right case.

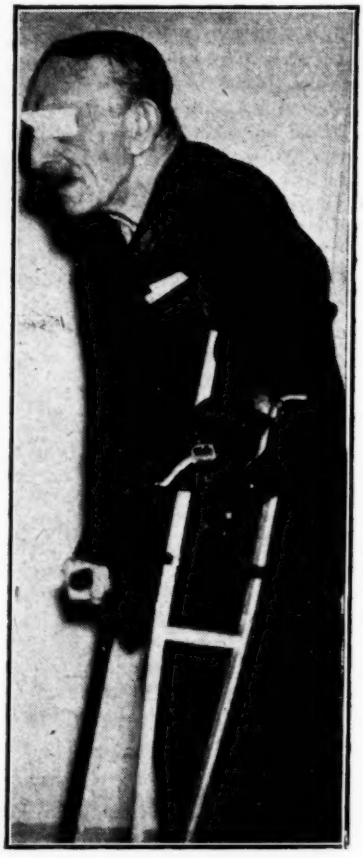


FIG. 3

Other exhibitors include the World Veterans Association, the Chartered Society of Physiotherapists, and the Association of Occupational Therapists, as well as departments of physical medicine and individual doctors and physiotherapists.

The exhibition demonstrates very clearly how self-help devices have developed along similar lines in different countries and at different centres. On the other side of the Atlantic there seems to be a tendency to encourage the use of aids at an earlier stage than in Britain : perhaps economic pressure demands this. At all events the Americans certainly lead in this field, especially where a complicated gadget is needed.

It may be hoped that the exhibition will stimulate the production of a comprehensive catalogue of self-help devices. This is badly needed, as at present information about them is widely scattered and certainly not easily available to the general practitioner.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Vitamin A in Bread

SIR,—Without wishing to involve you or myself in a discussion on the relative merits of "white" (that is, low extraction) and "brown" (that is, high extraction) bread, I venture to ask you not to perpetuate the long since disproved error that wheat flour contains any vitamin A. You do this in the annotation under the above heading (*Journal*, August 15, p. 385) when you say that "the processing of white flour" removes "practically all the vitamin A." Anyhow, it would be carotene in one or other of its biologically active forms, and not vitamin A, that would be present in purely vegetable material, but it was shown by Zechmeister and Cholnoky[1] more than twelve years ago that none of the carotenoids in wheat was identical with any of those known to have biological (vitamin A) activity, of which much the most important is β-carotene.

The carotenoids in vegetable and animal tissues are closely associated with, or actually dissolved in, the fatty material present; in wheat this is, for all practical puposes, confined to the germ and is the wheat-germ oil. The carotenoids of this oil were submitted by Zechmeister and Cholnoky to careful chromatographic fractionation and found to contain practically nothing but xanthophyll, which is devoid of all vitamin A action.

Readers who wish to check my authority for these statements can do so in any standard book on the carotenoids, such as that by Karrer and Jucker, translated by Braude.[2] They will find that these authors give the natural sources of different carotenoids. The sources given for α-carotene, β-carotene, γ-carotene, and cryptoxanthin, the only four biologically active carotenoids of importance, do not include wheat.

You, Sir, will, I am sure, support me in the view that it is especially wise to have one's facts right when discussing matters, such as the colour of bread, that seem to arouse irrelevant emotions.—I am, etc.,

Greenford, Middlesex. A. L. BACHARACH.

REFERENCES

1 *J. biol. Chem.*, 1940, **135**, 31.
2 *Carotenoids*. 1950. Cleaver-Home Press. London.

Gas Flows in Anaesthesia

SIR,—The article by Drs. G. Herington and E. James (*Journal*, August 8, p. 317) brings me to the point of making the following observations which, though they can scarcely be original, I have not yet seen anywhere in print.

It is common to read the statement in anaesthetic literature that anaesthesia was maintained with nitrous oxide–oxygen in the ratio 2:1 or 3:1, but generally no mention is made of the rates of flow of the gases. One assumes that the patient is intended to breathe a 3:1 mixture from the reservoir bag, but probably it was in fact the readings of the nitrous oxide and oxygen flowmeters which were in the ratio of 3:1, and this is not by any means the same thing. The larger the gas flows the closer does the ratio of the percentages of the gases in the bag approach that of the flowmeter readings. But with small flows, as used in closed-circuit-with-a-leak systems, this may be far from being so, because oxygen is metabolized at a variable rate and disappears from the system into the soda lime canister as carbon dioxide, whereas nitrous oxide, being inert, circulates continuously *once equilibrium has been attained*.

Now in the case in point nitrous oxide–oxygen anaesthesia was continued when "saturation with nitrous oxide was considered adequate . . . with 1 l. of nitrous oxide to approximately 300 ml. of oxygen . . .", which is a ratio of approximately 3:1. Assuming in this case a basal oxygen consumption of 200 ml./min., and equilibrium to be complete, the bag mixture would settle at 1,000/(300−200) or 10/1=9.1% O_2. Were the basal oxygen utilization only 50 ml. greater the ratio becomes 20/1=<5% O_2. To obtain an oxygen percentage equal to that of air requires either that the oxygen flow must be raised to 450 ml./min. (in this case), or that nitrous oxide be retained by the patient at the rate of 600 ml./min., which will only occur in the initial period of the anaesthesia. Doubling the flow rates to 2 l./min. and 600 ml./min. respectively, while leaving the ratio of flowmeter readings unchanged, raises the oxygen content of the bag mixture from 9.1% to 16.8%.

In practice, of course, one can only guess the oxygen consumption of a patient on the table. Thus it seems to me that in all cases it is important to note the actual rates of flow of the gases rather than the percentage of gases that the anaesthetist intended to administer.—I am, etc.,

Pewsey, Wilts. J. C. AINLEY-WALKER.

The Pain of Transurethral Manipulations

SIR,—I agree with your correspondent Dr. E. C. Atkinson (*Journal*, August 22, p. 440) that transurethral manipulations are extremely painful and distressing without adequate anaesthesia. Many years ago I came to the conclusion that in the male procaine and cinchocaine were very inadequate, and consequently whenever possible I used a general anaesthetic or a low spinal.

However, this has been changed by the introduction of lignocaine hydrochloride ("xylocaine"). A 2% solution kept in the urethra for 15 minutes gives a very satisfactory degree of anaesthesia. I now find it necessary to use a general anaesthetic only when I am treating by diathermy a growth or dealing with a nervous patient.—I am, etc.,

Ballygally, Co. Antrim. H. CALVERT DALES.

Generalized Actinomycosis with Possible Cardiac Involvement

SIR,—We thank Dr. Kevin Anderson (*Journal*, August 8, p. 340) for pointing out that *Actinomyces bovis* does not form spores. Nor, may we add, does it grow aerobically in *normal* methods of blood culture—that is why the spore-bearer grown aerobically was rejected.

We regret that our final generalization was argued to the particular, although we maintain that the principle put forward in our final paragraph still holds good.—We are, etc.,

RONALD S. SAVIDGE.
Bury. DONALD M. DAVIES.

Appendix in the Hernial Sac

SIR,—I should like to submit the following details of an uncommon case.

A healthy labourer, aged 62, was admitted to hospital on July 14, 1953, complaining of a large tender lump in his right groin. He had had bilateral herniae for 20 years controlled by an adder-headed truss. Some months previous to his admission he noticed the right side swell and "come down" but he did not bother to do anything about it in the way of medical treatment. Three days prior to admission he felt pain and tenderness which made him stop work and go to his doctor. On examination a lump 4½ by 3 in. (11 by 7.5 cm.) was found in the right groin in the position of the external ring. The skin over it was reddened and warm. The swelling was firm and it was impossible to get above it; there was an impulse on coughing and it was irreducible; it did not extend into the scrotum. The left external ring was weak and there was a cough impulse, but no visible lump. Bowel habits were normal and at no time had there been vomiting or abdominal pain.

The case was diagnosed as an irreducible right-sided hernia, probably omentocele and non-obstructed. At operation there was a large hernial sac which contained a gangrenous, grey-green coloured appendix, 7 in. (17.5 cm.) long. It was hard and contained several faecoliths. It was traced as far as the caecum, which was lying in the neck of the sac, and there ligated and excised in the routine manner. The sac was also ligated

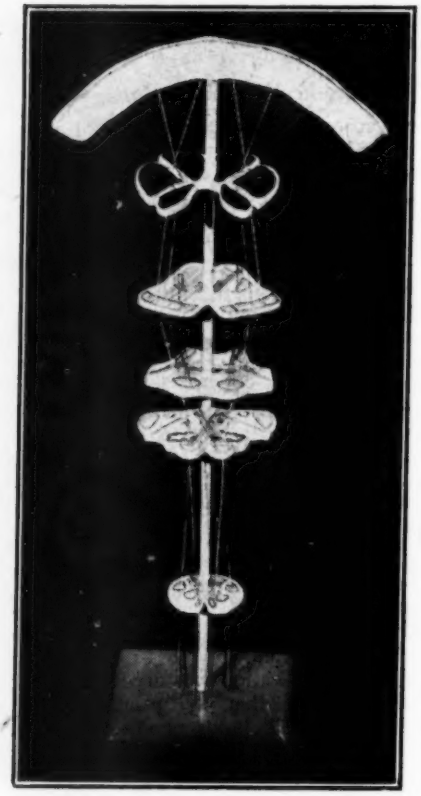
and excised, but no formal repair was carried out in view of the infected contents. The subsequent convalescence of the patient was uneventful and he was discharged home on July 28.

I have questioned several people, and, while they assure me they have heard of the occurrence, none can say they have seen such a case at operation. It would be interesting to know the frequency of the condition. I am grateful to Mr. J. A. O'Connell for his permission to publish the facts of the case and his help in the drafting of this letter.—I am, etc.,

Mullingar, Eire. T. E. WINCKWORTH.

A Visual Aid

SIR,—When I first studied neuro-anatomy as an undergraduate I found that I had become acquainted with various cross-sections of the brain and brainstem—but I had difficulty in visualizing these sections in relation to one another and especially in relation to the nervous tracts.



The photograph shows a model I have made which illustrates the pyramidal system in an attempt to clarify the formation of the internal capsule and the subsequent distribution of its crossed and uncrossed fibres. In this way, for example, it becomes more or less straightforward to show why the fibres from the lower part of the motor area *must* occupy the anterior position in the genu and thereafter lie medial to the remainder of the pyramidal tract in the midbrain. I feel that once the elementary conception of the interrelationship of the structures is grasped it becomes easier to know what one is looking for in the dissecting-room, and I venture to suggest that such a model would have cleared up many of the initial difficulties I encountered. Comments on its teaching value would be welcomed.

This model, in which coloured threads distinguish the various subdivisions of the pyramidal tract, was made with the help of my orderly, Bdr. J. Shaw, to whom my thanks are due.—I am, etc.,

Newcastle-upon-Tyne. J. G. COLLEE.

Spectacles

SIR,—I read with great interest Mr. J. H. Doggart's able review on spectacles (*Journal*, August 15, p. 388). I had feared that the art of spectacle prescribing was being relegated to the status of a merely technical accomplishment, and I derived much satisfaction from so authoritative a declaration that it is not so, and that it involves definite clinical, as well as technical, considerations. This needed saying, and Mr. Doggart is to be congratulated for saying it.

At the same time I think he may have gone too far in the direction of deprecating current views on the value of an eye examination in certain conditions, particularly headaches. It may be true to say that most headaches are not due to eye trouble, but I think it is a pity to suggest that many examinations for the exclusion of refractive errors are superfluous. The headache, it is true, may not be due to a refractive error, but it may be due to some other cause either of ocular origin or of some other origin showing ocular signs. I suggest that an examination of the eyes is an essential part of any thorough investigation into a case of headache of unknown origin. Also, I should like to suggest that the wearing of glasses gives relief from headaches in a great many patients whose headache is neither of refractive nor of heterophoric origin. Many such patients show signs of, or give a history of, conjunctival hyperaemia. This is aggravated by prolonged fixation, whether in driving, reading, or televiewing, and results in headache. Why glasses should give relief in such cases I do not know, but I have no doubt that they do, and I do not think that in most cases the relief is of psychological origin.

With regard to migraine, whilst I agree that it is not of refractive nor even of ocular origin, the diagnosis of the condition is not always a simple matter, so protean in its manifestations is it, and I think it is useful to have an ophthalmic examination in doubtful cases.—I am, etc.,

London, W.1. R. U. GILLAN.

SIR,—It is a pity that Mr. J. H. Doggart in his admirable exposition of the orthodox principles for prescribing spectacles (*Journal*, August 15, p. 388) has overstressed the dogma that headaches of ocular origin are uncommon and implied that only large refractive errors or those causing obvious symptoms need correction. This is unfortunate for two reasons: first, because it may hinder the recognition of some headaches which are easily relieved, and, secondly, because it weakens the true case against prescribing unnecessary spectacles. The suggestion that because large refractive errors often cause no discomfort small ones may not do so is misleading. Small errors probably cause more headaches than large ones, and a few people are acutely sensitive to visual imperfection although many are tolerant or indifferent to it.

As Mr. Doggart says, the history will usually supply a clue, but not if inquiry is limited to the effects of long spells of close work. There are two main sources of ocular fatigue—prolonged concentration and flickering lights. Watching the cinema, particularly a colour film, may give a useful guide to the effect of the latter. Ocular discomfort from the glitter of moving objects may be severe enough to provoke nausea and is responsible for one form of travel sickness. From my own experience I can aver that fishing rippling water on a bright day is a potent cause of headache, and had I realized this 25 years ago I could have avoided a grievous end to many an enjoyable day.

The question of migraine is more difficult. Headaches of ocular origin, especially those associated with ocular muscle imbalance, may cause vomiting and may thus improperly be labelled migraine. Their relief by spectacles has probably fostered the belief in the association of migraine with refractive errors. Of course, as Mr. Doggart says, migraine is not due to refractive errors—its fundamental cause is still unknown—but attacks may be provoked in those who are subject to it by many diverse stimuli, and it appears that, just as some are engendered by emotion, a few may follow ocular fatigue. It seems reasonable, therefore, to investigate this possibility when the history may suggest it.—I am, etc.,

Redruth. CHRISTOPHER HEATH.

Manual Methods in General Practice

SIR,—I would be grateful for the space in which to correct Dr. R. Barbor's misquotation (*Journal*, August 15, p. 395) from my letter (*Journal*, July 25, p. 222). Dr. Barbor writes that he cannot agree with my statement that "the proportion of total patients seen who require physiotherapy is 5%." That is not *my* statement. My actual words were :

"Only 5% of the total number (of patients) seen in that time were suffering from 'soft-tissue lesions.'" Of course I saw patients who required physiotherapy for arthritis of various joints, but these were not "soft-tissue lesions," while the physiotherapy they required consisted of methods of treatment other than "manual methods," which was the subject under discussion.

The relatively small number of patients I diagnosed as suffering from prolapsed intervertebral disk were suffering from prolapsed intervertebral disk, and the fact that they required to be seen and treated by a consultant orthopaedic surgeon confirms the severity of their condition. As I endeavoured to show in my letter, not all who have backache are suffering from prolapsed intervertebral disk.—I am, etc.,

London, N.W.3. PHILIP HOPKINS.

The Intervertebral Disk

SIR,—Disk injuries, and arthritis of the apophyseal joints, are part of the penalty man pays for his temerity in assuming an erect, plantigrade posture. Treatment should be based on this ontological conception: the child crawls before it walks. My routine of treatment, employed many years before the disk lesion was described, is: (*a*) three or four days in bed, with a firm pillow *tied* to the small of the back; (*b*) two weeks' hands-and-knees crawling for some 3 to 10 minutes three times a day; (*c*) two further weeks of hands-and-feet crawling, to strengthen further the erector muscles. With this technique manipulation is rarely required, the patient effecting the reduction himself by active movement. I usually give two or three paravertebral injections of lactic acid, with or without procaine, in the acute phases. Not infrequently, the relief of pain is dramatic, but I am somewhat sceptical of the Pauline conversion, as the patient is apt to give up the exercise too soon.

A few precautions may be mentioned. The knees should be padded and gloves worn. If postural scoliosis is present, crawling is done in a circle, away from the convexity. Outside the home the door should be locked: one patient circling his desk in this undignified attitude was surprised by his secretary—with disturbing consequences.

There is of course nothing original in this treatment, which is merely the adaptation of Klapp's exercises for lesser degrees of scoliosis. If it fails, the ruptured disk is almost certainly irreducible, and laminectomy is called for.—I am, etc.,

Sunderland. W. GRANT WAUGH.

Blood Transfusion Accidents

SIR,—I regret that the Consulting Pathologists Group Committee has prevailed on you to publish a "statement" (*Journal*, August 15, p. 390) on blood transfusion accidents. It is an anonymous statement, not even "approved" or "agreed" by the Group, and its authority is therefore nil—because the authority with which any "statement" is invested depends on the wisdom and experience of its authors. Unfortunately, non-medical readers are apt to assume that the wisdom of a medical committee is the sum of the wisdom of its members—whereas we know that their collective wisdom is rarely greater than their highest common factor.

In fact, the statement is inaccurate in some technical matters. Cross-matching in saline and albumin does not exclude incompatibility, because the antibody anti-Duffy fails to agglutinate Duffy-positive cells in saline or albumin, but can be detected only by the anti-globulin technique, which is not even mentioned in the statement. There is still some argument about the relative reliability of tile and tube methods for ABO grouping,[1 2] and it seems reasonably certain that the capillary method of Rhesus testing is not less reliable than is the tube method.[2 3]

Transfusion is intended to save lives, and in some hospitals transfusion is sometimes needed within 30 or 45 minutes, even now when dextran is freely used. I believe that there may be more than one technique which is reasonably safe in skilled hands, and I have the strongest objection to being told by some anonymous pundit that this is not true, the more especially when the pundit himself makes erroneous statements.

It is now generally accepted that most transfusion accidents are caused by bad organization, carelessness, or ignorance. The Group Committee might find it more profitable to represent to the Ministry, to regional boards, and to boards of governors that in no hospital should grouping and cross-matching be done in the ward sideroom by a house officer, but that in every hospital the organization of transfusion must be the responsibility of a consultant pathologist who has time, space, and staff to supervise the work properly.—I am, etc.,

London, N.W.10. GEORGE DISCOMBE.

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Heparin in Intravenous Infusion

SIR,—It is well known that difficulty is often experienced in maintaining a continuous intravenous infusion over a prolonged period owing to the onset of local thrombophlebitis, but it is much less well known how useful heparin can be in minimizing this complication. For several years I have used heparin with considerable success for this purpose. It may either be injected with a syringe into the flasks immediately before use or, alternatively, the flasks may be prepared in advance by the pharmacy department. A dosage of 1½ to 2 units per ml. of intravenous fluid is recommended. Using heparin in a strength of 1,000 units per ml., 0.75 to 1 ml. should therefore be added to each half-litre flask. If a stronger solution is used—for example, 5,000 units per ml.—the volume required for each flask is so small that it is difficult to measure accurately. Furthermore, it must be suitable for intravenous use. The risk of haemorrhage is not increased, because the heparin, administered in small amount and at a constant rate, has sufficient concentration only to act on the vein proximal to the needle or cannula. When it enters the general circulation it is too dilute to have any effect on the clotting time and is soon eliminated. It is safe to give heparin in this way shortly after, or even during, operation provided that the infusion has not to be run quickly. Should this become necessary, then the flask must be changed to one without heparin.

By this safe and simple method, time, painful thrombosis, and the consequent loss of a patent vein can be avoided. It is worthy of wider application.—I am, etc.,

Manchester. H. F. SMITH.

Familial Hypertrophic Pyloric Stenosis

SIR,—It was with great interest that I read the article by Mr. T. Fenwick on familial hypertrophic pyloric stenosis (*Journal*, July 4, p. 12). I recently had a similar case, though without an extensive family history. Perhaps it is worth recording briefly as another example of the type of association Mr. Fenwick has described.

The patient, a male aged 54, presented with an eight-year history of periodic lower sternal and epigastric pain, leading to nausea, and associated with acid regurgitation and vomiting. Recently there was loss of appetite and loss of weight. Radiologically he was diagnosed at two examinations as having a prepyloric ulcer with the possibility of malignancy. Exploration was advised. At operation there was a greatly hypertrophied pylorus which was thought at the time to be a tumour. A Billroth I type of gastrectomy was performed. The patient's subsequent convalescence was normal. Pathological examination revealed that the tumour showed a rather thin mucous membrane which was rather engorged and with more polymorphonuclear infiltration than normal, but no actual ulceration. The main abnormality, microscopically as well as macroscopically, was in the markedly increased thickness of the pyloric musculature. The individual muscle fibres themselves were abnormal, in that they were swollen and stained irregularly, giving the impression of being broken when viewed lengthwise, and of a ring shape when cut across. There also appeared to be marked separation by fluid of the individual fibres. No evidence of malignancy was seen. The conclusion was that it was pyloric hypertrophy.

When I discussed the findings with the patient and explained to him that the trouble had not been an ulcer but an enlarged muscle at the exit of the stomach causing obstruction, he said that his eldest child, a boy, had been rushed off at the age of 4 months to hospital and had had an operation for a similar condition. This has kindly been confirmed for me by the hospital concerned, which reports that the baby had a Ramstedt operation for pyloric stenosis at the age of 15 weeks.—I am, etc.,

Bath. S. GLASER.

Reduction of Post-operative Pain

SIR,—I read with interest the annotation (*Journal*, August 15, p. 385) concerning methods of relieving post-operative pain. Reference was made to the use of the drug "efocaine." It is true that this drug gives much longer anaesthesia than most of the other anaesthetics at our disposal, but it certainly has dangers and disadvantages. Three cases have been reported from America, where, following the use of efocaine, serious neurological symptoms developed and persisted, and it is understood that other permanent palsies have been encountered. In these cases intercostal injections have been made in the paravertebral region.

My registrars and I are at present investigating a small series of gastrectomies where the efocaine was injected in the region of the intercostal nerves in the mid-axillary line. In many of these cases the anaesthesia was very prolonged and has given considerable discomfort to the patient. We hope to publish a short account of these cases in the near future.—I am, etc.,

Liverpool, 1. J. B. OLDHAM.

Sun on the Skin

SIR,—In your annotation (*Journal*, August 8, p. 330) you mention that, although it is not easy to increase tolerance to light by systemic treatment, mepacrine by mouth delays the onset of erythema from ultra-violet light. No mention is made of nicotinic acid, which has quite a marked effect in the prevention of photo-sensitivity; a dose as small as 50 mg. per day has been successful in preventing the onset of light dermatitis in several photo-sensitive patients (for example, the dermatitis associated with pellagra).

You mention that sulphonamides increase sensitivity to light, and I find it rather interesting to speculate on the cause of the pharmacological antagonism between sulphonamide and nicotinic acid, which not only exists in bacterial infections but also in this matter of light sensitivity. Incidentally, I have learned by painful and personal experience never to apply creosote to wooden structures when the sun is shining; any stray drops landing on the skin cause the rapid development of an uncomfortable localized erythema.—I am, etc.,

London, W.1. R. J. GOURLAY.

Please Wash Your Hands

SIR,—I note with interest the letter from Dr. W. Edwards (*Journal*, August 22, p. 444) regarding free washing facilities in public conveniences. Two years ago I persuaded the Doncaster Health Committee to provided free hand-washing and drying facilities as an experiment in the men's convenience adjacent to the market, which is patronized by stallholders, the majority of whom are engaged in handling food. A wash-hand basin, soap dispenser, and electric hot-air hand drier were provided. The provision of such facilities is restricted to conveniences where an attendant is on duty in order to prevent misuse and damage, and the drier and soap dispenser have to be locked away when the attendant goes off duty, to prevent wilful damage. With these precautions I am pleased to be able to report that the equipment is still intact, is in daily use, and has proved popular. I might add that to reduce further the risk of spread of intestinal disease the flush controls of the w.c.s at this convenience were converted to foot operation in lieu of the usual hand control.—I am, etc.,

Doncaster. H. L. SETTLE.

SIR,—Your correspondent, Dr. W. Edwards (*Journal*, August 22, p. 444) in his letter on the washing of hands, raises a problem which deserves immediate attention. The fact that gastro-enteritis has become endemic and widespread is a sad reflection on the standards of hygiene and food management in this country. The time has surely come for a new drive for cleaner food.

Food-handlers require constant education and supervision. A revival of the system of granting hygiene certificates to cafés and food stores would be a good thing. The refusal of such certificates, and even closure of the more unsatisfactory establishments, would have a salutary effect on the raising of standards. The handling of articles ready to eat, such as sandwiches and cakes, should be forbidden when once prepared. They should be individually wrapped ready for sale. Our milk is now almost entirely delivered in bottles, and yet our bread loaves are rarely wrapped before delivery.—I am, etc.,

Carmarthen. J. E. CRANE.

Male Pseudohermaphroditism

SIR,—We have been interested to read the account of a case of male pseudohermaphroditism by Drs. D. C. Beatty, C. J. Champ, and G. I. M. Swyer (*Journal*, June 20, p. 1369). Owing to the rarity of such cases, mention of a similar one encountered by us some four years ago may be of interest.

The patient, a married woman aged 40, had always had amenorrhoea, but, except for the total absence of pubic and axillary hair, she had normal secondary sexual characteristics. As a child she had had treatment for a left inguinal hernia, and she was now admitted to hospital for repair of a right inguinal hernia. A tumour, shown histologically to be a testis, was removed at operation. No ovary or uterus could be felt through the hernial orifice, and bimanual examination showed a loosely attached vagina without a cervix or any nodule suggesting a uterus. The external genitalia were normal.

Further investigation could not be carried out as it was against the patient's wishes. She is one of a family of six girls; three are normal, married and with children; the other two are similar to the patient in that they have had permanent amenorrhoea, and one of them, who is married, has been told by a gynaecologist that she has no uterus.—We are, etc.,

GREGOR H. GRANT.
Shrewsbury. A. GLANDON WILLIAMS.

Treatment of Patients with Myelosclerosis

SIR,—Dr. R. A. Hickling's account of the clinical features of myelosclerosis (*Journal*, August 22, p. 411) does not refer to the remarkable duration of time of the pathological process in some cases. In 1950 I saw a man, aged 66, with enormous splenomegaly and fairly severe anaemia. A diagnosis of myelosclerosis was confirmed, and a number of transfusions were given which kept the patient alive for a further two years. A striking feature of this case was that great splenomegaly had been detected in 1910, when he was warned not to play football for fear of rupturing the enormous spleen. Apart from abdominal discomfort, no symptoms were noted until March, 1950, when he had a very severe epistaxis.

A man aged 53 was found to have a spleen reaching to the navel 12 years before I saw him. There were no other symptoms and no anaemia, but the leucocyte count was 35,400 with a few abnormal cells and an occasional normoblast. This patient is still in good health, with no treatment, 16 years after the splenomegaly was first noted.

It seems impossible to accept the view of Heller and his co-workers,[1] which is shared by Hutt *et al.*,[2] that such a prolonged disease could possibly be closely allied to the leukaemias. It is both interesting and important that Dr. Hickling observed improvement after irradiation of the enlarged spleen in cases with leucocytosis and immature cells in the blood. Obviously, therefore, the enlargement of the spleen, which has often been regarded as compensatory, is

not purely so, but his observations seem to support the view of Rohr[3] that the abnormal cells in this condition and in the leukaemias are mainly derived from the ectopic foci.—I am, etc.,

London, W.1. A. PINEY.

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2 *Blood*, 1953, **8**, 295.
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Subacute Bacterial Endocarditis

SIR,—Professor R. V. Christie in his Refresher Course article on subacute bacterial endocarditis (*Journal*, August 22, p. 438) mentioned penicillin used prophylactically before dental extractions. He says, and I agree that it is so, that the usual dose is 500,000 units "an hour or two" before the operation with a similar dose on the two succeeding days.

I have never been able to understand why my medical friends, fully aware of the disastrous nature of the disease, and the harrowing treatment of it should it occur, do not insist on heavy doses for several days before the operation in an attempt to reduce the number of bacteria in the foci before they are stirred up and disseminated by the operation.

By all means continue after the operation as well, but one dose only at some casually indefinite time beforehand seems to me very like locking the stable door after the horse (or the bacteria) has bolted.—I am, etc.,

London, W.1. F. R. COFFIN.

Symptoms of Malaria

SIR,—The recent correspondence in the *Journal* reminds me that I have frequently observed that the rigors and intermittent fever so characteristic of malaria tend to overshadow the fact that the first attack of malaria is not characterized by rigors and the fever is continuous. The second attack, which takes place six months later, is "classical" in its manifestations.

Gastro-intestinal symptoms frequently usher in an attack, being heralded by vomiting or diarrhoea, and patients who have been exposed to the infection and who present such symptoms should be suspect.—I am, etc.,

Northallerton, Yorks. J. SHEGOG RUDDELL.

Growth Hormone

SIR,—New information on endocrine factors influencing growth is accumulating with increasing velocity (*Journal*, August 15, pp. 353, 357, 383), and the time has probably come to be careful with the use of the term "growth hormone." Somatic growth is the final outcome of the interaction of a vast complex of agencies even in the intact animal; in the mutilated organism additional compensatory factors assume an important role in promoting or inhibiting growth. Thus, by suitable experimental interference, it is possible to demonstrate growth-promoting properties not only for somatotrophin and insulin, but also for thyroxine, cortisone, and testosterone, and consequently for thyrotrophin, gonadotrophin, and A.C.T.H. To call all these "growth hormones" would deprive the term of most of its usefulness. The term should be restricted to hormones having, in the *intact and normal* animal, a *direct* action on the somatic cells, in promoting protein synthesis and cell division.—I am, etc.,

Glasgow. E. GEIRINGER.

POINTS FROM LETTERS

Cortisone in Rheumatoid Arthritis

Dr. H. F. WEST (Sheffield) writes: Dr. C. L. Cope, in part two of his Refresher Course article on the use of cortisone and A.C.T.H. (*Journal*, August 8, p. 332), said of rheumatoid arthritis that "with such great benefit to be expected in the majority of cases it is clear that the case for cortisone is strong." Unfortunately the "case for cortisone" has not been made out and careful studies have brought no proof that it favourably affects the course of the disease. There is no doubt that many patients benefit from cortisone treatment temporarily, but there is also little doubt that in certain circumstances it may do more harm than good.

Obituary

RENÉ SAND, M.D., LL.D.

The death of Dr. René Sand on August 23 was briefly recorded in last week's *Journal*. For many years he was one of the most prominent figures in the field of social medicine, and his work achieved international fame.

René Sand was born at Ixelles, in Belgium, on January 30, 1877. He graduated in medicine at the University of Brussels in 1900, and after postgraduate studies in Berlin and Vienna was appointed lecturer in pathology at his own university. His interest in social medicine was developing even at this early stage of his career, and in 1912 he founded the Belgian Social Medicine Association. During the first world war he served as a medical officer to units of the Belgian Army, and in 1921 he was elected secretary-general of the League of Red Cross Societies, a position which he held until 1936.

Sand's interest in the international unification of medical services found many outlets in the period between the two world wars. He realized his ambition to found an International Hospitals Association in 1929, and he was its first president. He was also president of its post-war successor, the International Hospital Federation, from its foundation in 1947 until his death. Only a few months ago he was chairman of the Eighth International Hospital Congress in London. A tireless supporter of the health work of the League of Nations, Sand was naturally prominent in the councils of its post-war successor. In 1946 he presided over a technical preparatory committee of the United Nations Organization to study proposals for international action in the health field, and he was one of the Belgian delegates to the conference called in New York by U.N.O. to draw up the constitution of the World Health Organization. In 1950 he was appointed chairman of the W.H.O. Expert Committee on Professional and Technical Education. During the preparation by the International Labour Office of its Convention on Minimum Standards of Social Security, a special W.H.O. consultant group, with René Sand as its chairman, was appointed to review the medical provisions of the convention.

Sand's work to improve the health of his own countrymen was recognized by his appointment as secretary-general of the Belgian Ministry of Health in 1937. He was responsible for the opening of the Institute of Hygiene and Social Medicine in Brussels in 1939. After the war, with the support of the Rockefeller Foundation, a chair of social medicine was established in the University of Brussels, and Sand was its first occupant. He held this position from 1945 to 1952. He also founded the Belgium Committee on Social Work and the International Conference on Social Work, presiding over several of the meetings of the latter organization. Earlier this year he was elected the first president of the Société Belge de Droit International Médical, which has for its object the study and development of international medical law.

Sand was a member of the B.M.A. from 1917 to 1947, and an honorary member of the American Medical Association, the American Hospitals Association, and the New York Academy of Medicine. In 1951 he received the honorary degree of LL.D. at Glasgow Uni-

versity. He contributed many books and papers to the literature of his subject. Best known in this country is his *Vers la Médecine Sociale* (1948), an English translation of which, *The Advance to Social Medicine*, was published in 1952. This is a historical summary of social medicine, which he described as "the final flowering of the preventive and curative art," and a definition of its aims and methods. He also wrote *Health and Human Progress* (1935), *Un Programme de Santé pour la Belgique* (1945), and *La Médecine Sociale* (1950).

René Sand was one of the founders of the present-day concepts of social medicine: he had a unique grasp of his subject and a profound influence on its development outside his own country. His work was recognized by the award of the Léon Bernard Foundation Prize, which was presented to him at the Fourth World Health Assembly in 1951. He was to have been one of the vice-presidents at the First World Conference on Medical Education held in London last week, but illness prevented his attendance, and news of his death reached London while the Conference was in progress. The paper he was to have read as the introductory address to the section of the Conference considering preventive and social medicine was published in last week's *British Medical Journal* (p. 471).

We are indebted to Dr. MELVILLE DOUGLAS MACKENZIE, Chairman of the Executive Body of the World Health Organization, for the following appreciation: Apart from his exceptional personal charm and boundless enthusiasm, Dr. René Sand, an early pioneer in social medicine, had a breadth of vision that was almost unique. He will be long remembered not only for his conceptions of the potentialities of international collaboration in medicine but also for his ideas of the part that medicine, as an art, should play in the social structure of every country. He invariably looked beyond the ordinarily accepted, but relatively narrow, limits in the prevention of disease to the new and wide responsibilities of medicine in the complex social structure of modern life.

He realized, and lost no opportunity of urging, that the full development of medicine could only be reached if its social and psychological aspects received a proper place in the training of medical students.

His lovable personality and his zest for work, combined with his creative imagination, invariably gave him a position as leader in the many fields of national and international social work in which he laboured so incessantly. Chairmanship of the Technical Preparatory Committee for the creation of the World Health Organization, his long activities with the Red Cross, his work in the study of special social problems in many countries, including the United Kingdom and France, as well as his outstanding contributions to social work in his own country, gave René Sand the opportunities he sought, and brought to him the deep satisfaction of creative achievement. In 1951 the Governments of 66 countries formally recognized René Sand's contribution to social medicine when the Assembly of the World Health Organization unanimously awarded him the Léon Bernard Foundation Prize for his contributions to international health. On this occasion he concluded his address with the following words:

"Neither students nor practitioners fully realize that, as Hippocrates already said long ago, in medicine the function of protecting and developing health must rank even above that of restoring it when it is impaired.

"If the nobility of medicine resides in the selflessness of the physician, the hygienist, and their assistant, its greatness resides in the scope of the services which they render; and, from this point of view, the medicine which preserves health has a considerably greater influence for good than the medicine which restores health."

René Sand was a great man and one who was deeply loved by many colleagues in every country of the world.

J. T. HUNTER, F.F.A. R.C.S.

Dr. J. T. Hunter, who held a number of appointments as an anaesthetist at hospitals in and near London, died after a long illness on August 9 at the age of 54.

John Trustcott Hunter was born on September 4, 1898, and received his medical training at St. Bartholomew's Hospital, qualifying M.R.C.S., L.R.C.P. in 1925. He held the appointment of senior resident anaesthetist at St. Bartholomew's Hospital from 1926 to 1928, after which he was in general practice in the London area for some years. He then decided to specialize as an anaesthetist, and the list of hospitals he served is an impressive one. At the time of his death he was honorary consulting anaesthetist to the Metropolitan Hospital; King George Hospital, Ilford; King Edward VII Sanatorium, Midhurst; the Hospital for Tropical Diseases, London; and the Lord Mayor Treloar Orthopaedic Hospital, Alton. Earlier he had held the appointments of senior consultant anaesthetist to the Prince of Wales's General Hospital, Tottenham, and honorary anaesthetist to a number of other London hospitals. Hunter obtained the Diploma in Anaesthetics of the English Royal Colleges in 1944, and four years later he was elected a Fellow of the Faculty of Anaesthetists of the Royal College of Surgeons of England.

In 1939 he was appointed consulting anaesthetist to the plastic surgery and jaw injuries centre at the Queen Victoria Hospital, East Grinstead, where, perhaps, his warm sympathy for all who suffered showed itself most clearly. There he helped patients from some 14 different nations who had suffered facial injuries in the last war to regain faith in themselves and in the future by his constant encouragement and help. A founder member of the Guinea Pig Club at the hospital, he held the affection of all at East Grinstead, where he was known as "Uncle John."

Hunter had been seriously ill for nearly a year before his death, which took place in the hospital at East Grinstead. Big in stature and in mind, he was a born raconteur and an excellent mimic and could be relied upon to enliven any gathering by his presence. His death leaves a gap which will be difficult to fill. The sympathy of all his friends, colleagues, and patients will be extended to his widow.

We are indebted to Dr. A. A. MASON for the following appreciation: All who knew John Hunter have lost a dear friend. Of his professional capabilities, I will say little, for they have long spoken eloquently for themselves. If there was a difficult child to anaesthetize, we sent for John, and watched his gentle induction with pleasure and envy. If a small child was afraid, it was Uncle John who soothed it, turned its tears to smiles and peaceful unconsciousness. If an endotracheal tube would not obey our behest, it was John who guided our fingers. He was an anaesthetist by instinct. He did not attempt to explain why he did things correctly, he just did them. We younger anaesthetists knew the latest theory, but he knew much more—the practice of safe anaesthesia. If the anticipation of trouble is the mark of the good anaesthetist, then John was the prince of all, for he smelt trouble and prevented it before we were even mildly suspicious. His record speaks for itself—3,000 cleft-lip and palate operations over 20 years with the loss of only one child—a record that few will ever equal.

It is, however, as a man that we will miss him most. His geniality and generosity were unsurpassed. An evening with John was an evening of good food, good wine, and robust humour. John enjoyed life and lived it to the full. He was happiest when taking his friends down the river and making them merry. His dinner parties will long be remembered,

for he was a host who gave everything, most particularly himself. My last memory of John—and this was even after he had become seriously ill—was of him standing on the hearth, glass in hand, and surrounded by laughing, happy people; and it was John making them so. One of the best anaesthetists of his day, a man who enjoyed life and lived it well, a raconteur without peer, a man who hurt no one, a man one could always turn to in need, John was an institute—we shall rarely see his like again.

A. SMITH POOL, L.R.C.P.Ed.

We record with regret the death of Dr. A. Smith Pool at his home at Glasgow on August 16 at the age of 59 after a short acute illness.

Alexander Smith Pool was born at Annan on October 13, 1893, and was educated at Annan Academy. He left Dumfriesshire for Glasgow as a young man and in 1914 qualified as a member of the Pharmaceutical Society of Great Britain: it was typical of his industry and application that, although compelled by circumstance to seek part-time employment throughout his period of study, he qualified as a pharmacist before the statutory age of 21. With great courage he commenced business on his own account shortly after qualification, and by working long hours had soon established a flourishing business in one of the industrial areas of Glasgow. In 1919 he again showed his courage by beginning the study of medicine at Glasgow University. After he had completed his first year there circumstances compelled him to transfer to the Anderson College of Medicine—a forced decision which he always regretted. He was still conducting his business, and hurried from his classes to his dispensing every day of the week. On most evenings he left his business between 10 and 11 p.m. to pursue his medical studies till the early hours of the morning. However, he did well at the Anderson College and obtained the Scottish triple qualification in 1926 and secured the appointment of extra-dispensary physician to the Victoria Infirmary, Glasgow. In 1931 he was elected physician to out-patients. He was at first attached to the wards of the late Dr. O. H. Mavor (James Bridie), who appreciated his colleague's worth and frequently referred to Pool's knowledge of pharmacology and "its sane application to treatment." Dr. Pool enjoyed his out-patient duties, and was seen at his best surrounded by a group of students, his eyes sparkling, as he instructed them in the arts of percussion and auscultation.

Early in his medical career Dr. Pool took an active interest in medical politics, and was soon recognized as a good committee man. He graduated quickly to fill with distinction all the positions to which his colleagues could promote him. He was president of the Glasgow and West of Scotland Branch of the British Medical Association at the time of his death; chairman of the Glasgow Division in 1946–7; and from 1943 to 1951 he was a representative of the Division at seven Annual Representative Meetings. He was a member of the Central Council of the Association from 1945 to 1948, and at various times since 1943 he had served on the Scottish Committee, the Scottish Insurance Acts Subcommittee, the joint committee of the B.M.A. and the Pharmaceutical Society, the Joint Standing Formulary Committee, and the General Medical Services Committee and the G.M.S. Scottish Subcommittee. He had also been chairman of the Glasgow burgh panel and local medical committee. Recently he was a member of the Cohen Committee on Prescribing, an appointment of which he was proud.

Alec Pool was forceful and courageous in debate; he hit hard, but without rancour. After a particularly stormy session he would seek out his opponents and, amid laughter, count the points scored on each side. He was most jealous of the position of the doctor in the community. His experience and knowledge of business were such that at times he showed little respect for lay members of committees who presumed to criticize the work of the general practitioner. As one who had been successful in both business and medicine he had no doubts regarding which was the easier to attain. He was appalled by the recent increase in litigation against doctors, and proved himself a formidable opponent to those malcontents who made official complaints against their medical attendants. He never quite adjusted himself to the National Health Service, and only a few weeks before his death he was actively prospecting farming properties to which he looked forward to retiring in a short time. The wheel had come full circle, for he was at heart a countryman and was reared on a farm at Annan. He had only three interests—the practice of medicine, medical politics, and farming; he was eminently successful in two of these fields, but, alas, the third escaped him. The sympathy of his colleagues and friends goes out to his wife and only daughter.—A. B.

After a comparatively short illness, which she endured with her customary fortitude, Dr. ROSEMARY OWEN MORRIS died at Caernarvon on August 15 at the age of 60. Born on June 21, 1893, she was the daughter of the late Dr. R. Owen Morris, of Aberdovey, who was well known throughout the Principality as the active propagandist of the Welsh Tuberculosis Association. After studying music and teaching the subject for a few years, she later became a medical student and obtained the degrees of M.B., Ch.B. at Edinburgh University in 1920. Two years later she took the diploma in public health, and in 1928 proceeded to the M.D. The public health service soon attracted her, and she held posts at Huddersfield, Norwich, and the Cefn Mably Sanatorium, near Cardiff. In 1950 she joined the Caernarvonshire health department and was a most loyal and energetic colleague. A member of the British Medical Association and the Society of Medical Officers of Health, she was also a keen supporter of the North Wales Branch of the Medical Women's Federation. She possessed an abounding sense of humour and always had a cheerful greeting for her colleagues. All her colleagues mourn the loss of a sweet personality whom they admired and respected.—D. E. P.-P.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

In Congregation on June 23 and 24 the following medical degrees were conferred:

M.CHIR.—*G. C. Attenborough.

M.B., B.CHIR.—*J. Cocker, *H. E. D. Lloyd, *J. E. C. Tower, *D. B. Bower, *R. A. Miley, *R. A. Roxburgh, *J. L. Stevens, A. J. F. Barratt, R. M. Butcher, H. F. Cowper Johnson, R. J. W. Lambert, M. B. Teal, *P. M. Hacking, *M. B. Heywood-Waddington, *A. R. Kittermaster, *I. B. Lyon, *A. McL. Keil, *P. C. Vivian, *C. M. Yates, *E. R. Davies, *J. P. F. C. Evans, *R. V. H. Jones, *J. S. Lloyd, *W. O. McCormick, *G. Meachim, *D. G. Montefiore, *P. H. Pullen, *I. R. D. Reid, *N. W. H. Young, *A. B. Aistrop, *T. C. Bradford, *M. J. Clarke-Williams, *I. M. J. Mair, *R. Routledge, D. W. Couch, A. H. Dimond, P. W. Hayward, J. McM. Mennell, H. G. Penman, *V. G. Caiger, *R. H. Champion, *K. Coventry, *E. J. Cretney, *M. G. A. Forrest, *R. Gardner, *A. F. Hignell, *J. A. Holland, *E. O'G. Kirwan, *D. G. Lethem, *R. J. Sellick, D. Campbell, D. N. M. Goodson,, H. R. M. Johnson, A. C. Markland, P. Sleight, G. C. E. Wilson, *R. V. Jones, *J. A. McEwan, *B. A. Maurice,

*M. J. Mynott, *M. J. Pritchard, *M. C. Guard, *J. E. Lennard-Jones, *N. D. Mackichan, *A. B. Myles, *N. P. Burns, *G. M. Cochrane, *P. F. Dixon, *B. G. Gradwell, *I. Lenox-Smith, *N. V. D. Bunker, *P. M. E. Dutton, *C. B. Hobbs, *M. V. J. Fitzgerald, *R. W. Hall, *H. T. Thomas, *R. J. Vaughan, *P. Wellings, M. J. W. Penn, *G. D. H. Shephard, *H. J. Hodgson, *A. J. Kenmuir-Evans, *J. M.Clifford, *J. E. Goodess, *M. B. Harris, *A. F. Madge, *R. K. Waterhouse, *M. Trede, R. J. Daniels, *Judith M. Fitzsimons, *Beryl P. Jones, *Thérèse M. Vanier, *Sheila M. Houghton, *Ruth Hutchinson, *Joy Paterson, *Inez M. P. Smeed, *Elizabeth H. M. Walker, *J. B. Carver, *D. M. Davies, *M. Heslop.

In Congregation on July 13 the honorary degree of ScD. was conferred on Harold Robert Dew, Bosch Professor of Surgery and Dean of the Faculty of Medicine in the University of Sydney.

*By proxy.

UNIVERSITY OF DURHAM

In Congregation on July 3 the following medical degrees were conferred:

M.D.—J. P. Anderson, T. Bird, Ruth M. Dearing, D. H. Turnbull, *T. Manners, *W. M. Ross.

PH.D. IN PURE SCIENCE.—Phyllis A. Armstrong, M.B., B.S.

M.B., B.S.—J. Baldasera, J. Beveridge, Barbara H. Brown, W. D. Busby, C. E. Camm, M. D. Cashman, Margaret E. Chitty, D. E. Clare, K. M. Coia, W. G. Cooke, N. E. Crumpton, A. A. Darkwa, J. Deegan, K. A. Delpeche, T. F. Dias, P. R. Dingle, T. Dowell, G. W. H. Fisher, M. L. Fisher, J. B. Foster, W. D. Glass, A. H. Grabham, J. P. Graham, Jean H. Graham, W. Graham, K. C. Grant, E. A. Haddock, Thelma Haddock, J. N. Harkness, J. D. Heaton, K. N. Henderson, R. J. Henry, J. M. Hipkin, Mary E. Hobson, Elizabeth A. Hopkinson, S. R. Hutton, N. J. Jackson, G. L. Johnston, Jane M. Lee, J. A. Little, Beatrice M. Lowry, J. F. Lund, H. Madgwick, G. N. Marsh, J. F. Milligan, Joyce M. Mitcalfe, Mary J. Mossman, E. Muris, R. S. Parsons, H. G. Pledger, J. Ridley, P. F. Roythorne, Marion Rutter, R. P. Ryan, G. Safe, W. E. Seales, D. H. Spark, H. S. Spiller, Pat E. Stephenson, Doris Story, D. Strachan, C. W. Thomson, M. E. Tulloh, H. A. S. Walker, Daphne Warner, R. B. Welch, F. W. Woodruff, *D. C. Dove, *H. T. John, *Ione M. Martin, *T. H. Oglesby.

In absentia.

UNIVERSITY OF BIRMINGHAM

In Congregation on July 4 the following degrees were conferred:

M.D.—R. L. Bishton, A. B. Black, J. T. A. George, W. C. Smallwood, Hebe F. Wellbourn.

PH.D.—W. St. C. Symmers, M.D., M.R.C.P. (*in absentia*).

M.B., CH.B.—P. J. F. Aaronricks, Betty A. Astle, Patricia Baker, P. Beavon, Irene M. Bidwell, P. W. S. Blake, M. B. Bottrill, A. J. Bray, R. C. Brown, R. MacA. Brown, Jennifer Browne, Anne F. Calladine, A. R. Chrispin, Elinor B. Clark, D. B. Clarke, G. K. Clarke, K. A. Cowan, J. D. Cumming, I. J. Cunningham, T. P. Daly, Doris M. Davies, R. Davis, W. K. Eltringham, [1]S. E. Evans, J. Farrington, Frances J. Folley, Patricia A. Gough, L. A. Green, D. D. Griffiths, A. B. Guest, G. G. Habib, W. P. Hayne, R. N. Hill, K. C. B. James, Verna S. James, Julie Jones, Mary F. Knight, P. R. Knight, Kathleen M. Lumb, Dorothy M. Mahabir, D. P. Mason, M. D. Ma'tuk, Hazel R. Meacock, D. B. Minton, [2]S. Naimi, G. D. Oates, W. J. O'Connell, G. D. Parbrook, M. D. Parker, H. G. Parkes, J. B. Pearson, T. P. Perry, [1]B. Purdy, C. O. Quarcoopome, C. C. G. Rawll, Gweniver W. Roberts, M. H. Rogers, Pamela M. Rose, G. H. Shaw, G. Singh, S. H. Taylor, Sheila M. Topping, [1]D. Vuckovic, A. J. Wainwright, P. J. C. Walker, A. D. Wardle, J. Warner, B. Watson, D. G. Williams, P. M. Wine, P. E. Woods, [2]P. N. Wormald, A. Yeadon.

[1]Distinction in paediatrics and child health. [2]Distinction in medicine.

The Services

Major-General R. D. Cameron, C.B., C.B.E., M.C., late R.A.M.C., retired, has been appointed Colonel Commandant, R.A.M.C., in succession to Major-General (Honorary Lieutenant-General) Sir T. O. Thompson, K.C.S.I., C.B., C.B.E., whose tenure has expired.

Surgeon Commander S. M. Whitteridge, R.N.V.R., and Surgeon Lieutenant-Commander D. A. Warden, R.A.N.R., have been awarded the Royal Naval Volunteer Reserve decoration.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending August 15 (No. 32) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	22	1	3	0	3	19	2	8	0	
Dysentery	217	34	65	2	3	119	22	69	2	6
Encephalitis, acute	8	1		1		4	2	0	0	
Enteric fever:										
Typhoid	10	0	0	0	0	4	0	3		1
Paratyphoid	10	0	0	0		62	1	1(B)		0
Food-poisoning	389	21		2		150	21		0	
Infective enteritis or diarrhoea under 2 years				10	44				14	39
Measles*	2,123	67	24	41	26	7,010	926	47	68	146
Meningococcal infection	31	1	16	2		18	0	8	2	2
Ophthalmia neonatorum	32	2	9	0		19	3	10	0	
Pneumonia†	238	13	117	2		239	12	118	4	
Poliomyelitis, acute:										
Paralytic	186	14	17	8	12	167	16	8	6	1
Non-paralytic	132	3				83	8			
Puerperal fever§	322	38	17	2		242	44	11	0	
Scarlet fever	488	25	109	22	31	720	72	121	9	34
Tuberculosis:										
Respiratory			124	21				133	16	
Non-respiratory			18	7				25	2	
Whooping-cough	4,681	428	303	49	69	1,766	97	92		114

DEATHS in Great Towns	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	0	0	0		0	1	0		0	0
Dysentery	0	0				0	0			
Encephalitis, acute		0			0		1			0
Enteric fever		0	0			1	0		0	
Infective enteritis or diarrhoea under 2 years	9	2		1	1	4	1	1	1	0
Influenza	2	0	0	0	0	3	1		0	0
Measles		0	0		0		1		0	0
Meningococcal infection		0	0				0			
Pneumonia	116	22	17	9	4	134	9		4	5
Poliomyelitis, acute	9	2			0	8	3			0
Scarlet fever		0	0		0		0		0	0
Tuberculosis:										
Respiratory	78	10	11	1	6	74	16	14	1	6
Non-respiratory		1	0	0	2			2	0	2
Whooping-cough	2	0	1	0	0	0	0		0	0
Deaths 0–1 year	209	25	33	5	6	195	17	23	10	8
Deaths (excluding stillbirths)	4,500	648	483	93	12‡	3,962	583	478	91	116
LIVE BIRTHS	7,861	1213	857	203	466	7,209	1078	916	211	335
STILLBIRTHS	208	29	20			163	14	14		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

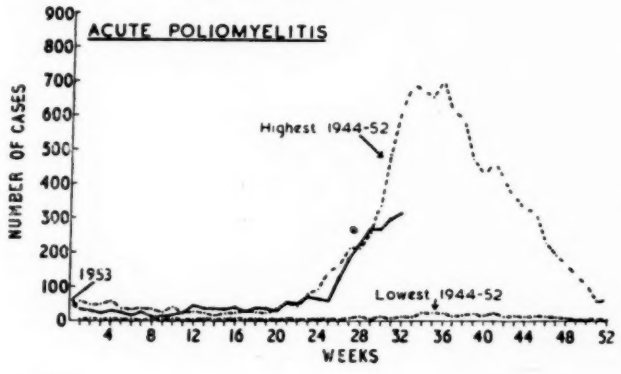
Poliomyelitis

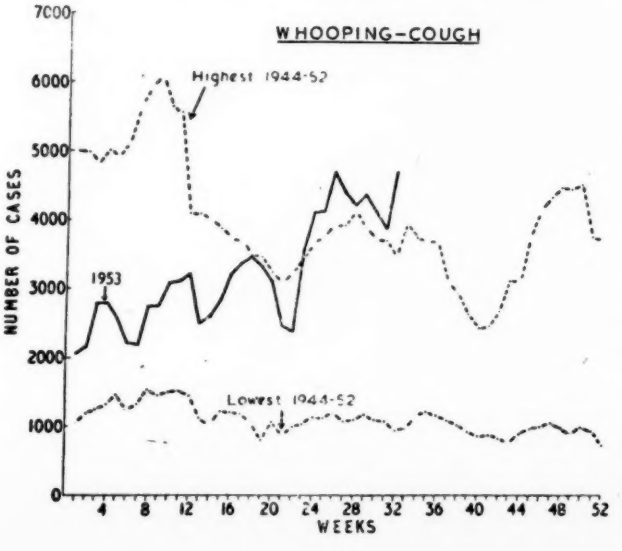
Poliomyelitis notifications (uncorrected) in the week ended August 22 (33rd week of the year) were as follows: paralytic, 144 (186); non-paralytic, 126 (132); total, 270 (318). This is a decrease of 48 compared with the previous week, the figures for which are in parentheses. The individual districts which have notified 20 or more cases in the year to August 22, with incidences per 100,000 in parentheses, are as follows: Southend-on-Sea C.B., 43 (28.38); Liverpool C.B., 51 (6.44); Birmingham C.B., 55 (4.92); Coventry C.B., 108 (41.38); Leicester C.B., 28 (9.79); Lewisham M.B., 24 (10.57); Blackpool C.B., 24 (16.29); Camberwell M.B., 21 (11.59); Islington M.B., 24 (10.20); Bournemouth C.B., 31 (22.32); Bristol C.B., 21 (4.73); Nottingham C.B., 23 (7.40); Taunton M.B., 25 (72.25); St. Pancras M.B., 23 (16.48); Carlisle C.B., 22 (32.40); and Manchester C.B., 20 (2.83).

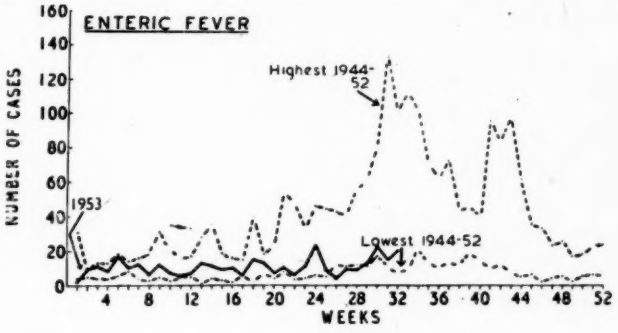
There were 48 fewer notifications during the 33rd week than during the 32nd. This decrease, occurring before the zenith was to be expected, is encouraging, particularly as the fall is most marked in the number of paralytic cases (42 less). There is still no sign of dangerous epidemic foci in the larger centres of population.

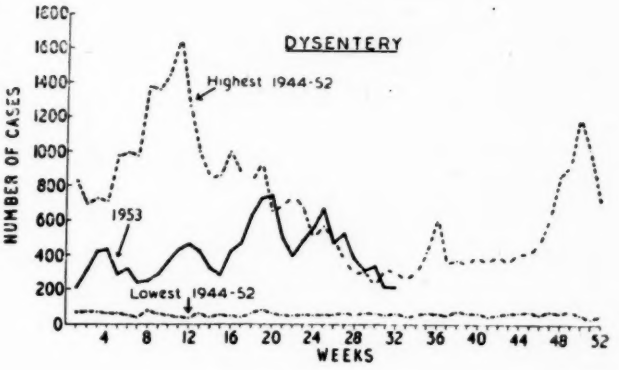
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The largest fluctuations in the trends of infectious diseases in England and Wales during the week ending August 15 were decreases of 607 in the number of notifications of measles, from 2,730 to 2,123, and 202 for scarlet fever, from 690 to 488, and an increase of 817 in the number of notifications of whooping-cough, from 3,864 to 4,681.

The largest falls in the notifications of measles were 149 in Lancashire, from 461 to 312; 91 in Lincolnshire, from 195 to 104; and 57 in Wiltshire, from 94 to 37. The decline in the incidence of scarlet fever was due to small falls in most areas of the country; there were no large fluctuations in the local trends. The largest rises in whooping-cough notifications were 106 in Yorkshire West Riding, from 232 to 338; 79 in London, from 349 to 428; and 70 in Hertfordshire, from 79 to 149; 22 cases of diphtheria were notified, the same number as in the preceding week.

318 cases of acute poliomyelitis were notified, and these were 5 more for paralytic and 16 more for non-paralytic cases than in the preceding week. The largest returns were Warwickshire 36 (Coventry C.B. 21, Nuneaton M.B. 5, Birmingham C.B. 4), Lancashire 31 (Liverpool C.B. 20), Essex 19 (Southend-on-Sea C.B. 5), London 17 (St. Pancras 4), Kent 16, Sussex 16, Southampton County 15 (Bournemouth C.B. 4), Dorset 12 (Poole M.B. 4), and Middlesex 12.

217 cases of dysentery were notified during the week—the same number as in the preceding week. The chief centres of infection were Lancashire 45 (Liverpool C.B. 11), London 34, Middlesex 16, Yorkshire West Riding 14, Surrey 11 (Epsom and Ewell M.B. 10), and Kent 11.

Northern Ireland Quarterly Return

The Northern Ireland Registrar-General, in his return for the quarter ended March 31, 1953, records that the birth rate was 21.3 per 1,000 population, being 0.5 higher than March quarter 1952, and that the death rate was 13.4 per 1,000 population—an increase of 0.4 over the corresponding quarter last year, but 1.3 below the average rate for the first quarters of the five years 1948–52. The higher death rate in March quarter 1953 was mainly due to an increase in the number of deaths from the respiratory diseases, especially influenza, pneumonia, and bronchitis. The death rate from tuberculosis, which has continued to fall, was returned at 32 per 100,000 population, a decrease of 8 com-

pared with March, 1952, and the lowest record for March quarter of any year. One death was registered as due to diphtheria—the first from this disease since June quarter 1951. The number of cases notified was 3 as compared with 2 for the first quarter of 1952.

Week Ending August 22

The notifications of infectious diseases in England and Wales during the week included scarlet fever 431, whooping-cough 4,341, diphtheria 11, measles 1,558, dysentery 235, paratyphoid fever 7, typhoid fever 3, and food-poisoning 339.

Medical News

White Bread.—Statutory Orders which came into force on August 30 have removed the restrictions on the extraction rate of flour, thus permitting a return to the white loaf. The Orders require, however, that calcium in the form of creta praeparata (1 oz. to 20 lb.—1 g. to 320 g.) shall be added to all flours; and that iron, aneurin, and nicotinic acid shall be added to flours of extraction rate lower than 80%, the rate for national flour. Only bread made from national flour remains controlled in price.

Artificial Sweeteners in Food.—In future only saccharin will be permitted as an artificial food sweetener (Artificial Sweeteners in Food Order, 1953). This follows a recommendation from the Medical Research Council. Saccharin is known to be harmless, but according to the Council's Food Adulterants Committee the use of certain other artificial sweetening agents may be dangerous to health.

Edridge-Green Lectures.—The late Mr. F. W. Edridge-Green, who was internationally distinguished for his work on the testing of colour vision (see *Journal*, May 2, p. 998), has left £3,000 to the Royal College of Surgeons. The money is to form a fund to pay for lectures at the College, "to be called 'The Edridge-Green Lectures,' one lecture each year to be on vision or colour vision."

Local Registration in East Africa.—The Uganda Legislative Council has approved a Bill enabling those who obtain the qualification L.M.S. (E.A.) from Makerere College to be registered for medical practice anywhere in East Africa. Before full local registration is granted, however, two years must be served as an intern at an approved hospital, and, after registration, five years in the Government medical service. Dr. J. K. Hunter, who moved the new Bill in Legislative Council, recalled that two years previously the General Medical Council had sent a delegation of visitors to examine the standard of training at Makerere. As a result of what they saw, they had recommended that the Makerere qualification might well become locally registrable. Dr. Hunter added that this was a step towards full recognition by the G.M.C.

Van Meter Prize Award.—The Van Meter Prize Award of $300 is again offered by the American Goitre Association for the best essays submitted describing original work relating to problems of the thyroid gland. Essays should not exceed 3,000 words in length, and a typewritten copy, in duplicate and double spacing, should be sent to the Corresponding Secretary of the Association, Dr. John C. McClintock, 149½ Washington Avenue, Albany 10, New York, not later than January 15, 1954. The award, which is open to both medical and non-medical workers, will be made at the Annual Meeting of the American Goitre Association in Boston, Massachusetts, next April.

Journal Index.—The half-yearly indexes to Volume I of the *Journal* and the *Supplement* for 1953 are now being sent to members who receive them regularly and to subscribers. Members who have not previously asked for the indexes can obtain copies, post free, on application to the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Mr. St. J. D. Buxton is leaving for Greece on September 7. He is going there at the invitation of the United Nations Organization to act as social welfare adviser. He will be away for about a month.

COMING EVENTS

The St. Thomas's Hospital Old Students' Dinner will be held at the Connaught Rooms, Great Queen Street, London, W.C.1, on October 2 at 7 p.m. The chair will be taken by Sir Henry Letheby Tidy. Tickets for the dinner (price 22s. 6d.) may be obtained from the secretary, St. Thomas's Hospital Medical School, London, S.E.1.

Symposium on Child Health in the Tropics.—Immediately following the seventh International Paediatric Congress (Havana, October 12 to 17) a symposium on Child Health in the Tropics will be held at the University College of the West Indies, Mona, St. Andrew, Jamaica, from October 20 to 27. Those wishing to attend or requiring further information are asked to communicate with the secretaries, Symposium on Child Health, Division of Medicine, University College of the West Indies, Mona, St. Andrew, Jamaica, B.W.I.

NEW ISSUES

British Journal of Ophthalmology.—The next issue (Vol. 37, No. 9) will be available in a week's time. The contents include:

ROLE OF OXYGEN IN THE GENESIS OF RETROLENTAL FIBROPLASIA. A PRELIMINARY REPORT. Norman Ashton, Basil Ward, and Geoffrey Serpell.
EARLIEST SYMPTOMS OF DISEASES OF THE MACULA. Marc Amsler.
VISUAL ACUITY AND THE CONE CELL DISTRIBUTION OF THE RETINA. E. R. Harrison.
PLASMA CELL MYELOMA OF THE ORBIT. Edwin Clarke.
CHANGES IN THE REFRACTIVE POWER OF THE CORNEA DURING GROWTH. OBSERVATIONS ON THE RABBIT. Arnold Sorsby and Michael Sheridan.
CURARE AND CURARE-LIKE PRODUCTS IN CATARACT SURGERY. L. P. Agarwal.
PENETRATING CORNEAL GRAFT. ORIENTATION OF THE INITIAL PENETRATION OF THE TREPHINE INTO THE HOST CORNEA. I. C. Michaelson.
DETECTION OF GLAUCOMA IN GENERAL PRACTICE. F. A. Williamson-Noble.

Issued monthly; annual subscription £4 4s., single copy 8s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

APPOINTMENTS

BLOTT, T. D., M.B., B.S., D.P.H., Assistant County Medical Officer and Medical Officer, Hucknall Urban District Council, Nottinghamshire.

MCDOUGALL, JOSEPH HENRY, M.B., Ch.B., D.P.M., Medical Superintendent and Consultant Psychiatrist, Moss Side Hospital, Maghull, near Liverpool.

MANCHESTER REGIONAL HOSPITAL BOARD.—I. MacD. G. Stewart, M.D., M.R.C.P., Consultant Physician, Victoria Hospital, Blackpool; J. G. Thurston, M.B., B.Chir., M.R.C.O.G., Consultant Obstetrician and Gynaecologist, Blackburn and District Hospital Centre; T. D. Culbert, M.B., Ch.B., D.A., Consultant Anaesthetist, United Manchester Hospitals and North Manchester Hospital; D. C. Lindars, M.B., Ch.B., Tuberculosis Physician and Medical Officer in charge of Miniature Mass Radiography Unit based on Salford; J. Rimington, M.B., Ch.B., Tuberculosis Physician and Medical Officer in charge of Miniature Mass Radiography Unit based on Stockport.

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—G. O. Storey, M.B., B.Chir., M.R.C.P., D.Phys.Med., full- or maximum part-time Consultant Physician in Physical Medicine at hospitals and clinics within the Central and Hackney Groups.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Boucher.—On August 18, 1953, at Dorchester, Dorset, to Betty (formerly Thompson), wife of P. R. Boucher, a son.

Davies.—On August 22, 1953, at the Bromhead Maternity Home, Lincoln, to Eva, wife of Dr. Hartley Davies, of High Barn, Welton, Lincoln, a son.

Lucas.—On August 26, 1953, at Bristol Maternity Hospital, to Mary (formerly Campbell), wife of Dr. George Lucas, a daughter—Angela Jane.

Reilly.—On August 24, 1953, at the London Hospital, London, E., to Joy (formerly Petrie), wife of Michael Reilly, M.S., F.R.C.S., a son—Christopher Michael.

DEATHS

Clarke.—On August 3, 1953, at Pine Cottage, Foxford, Co. Mayo, Eire, Isaac Clarke, L.R.C.P.&S.I.&L.M., late of Slough, Bucks.

Horne.—On August 10, 1953, at the City Isolation Hospital, Lincoln, Hugh Wilson Horne, L.R.C.P.&S.Ed., L.R.F.P.S., D.P.H.

Mead.—On August 16, 1953, at "Bryn-y-Mor," Yarmouth Road, Lowestoft, Suffolk, John Clarke Mead, M.B., F.R.C.S., aged 72.

Pollock.—On August 4, 1953, at East London, South Africa, Andrew Maclean Pollock, M.B., F.R.C.S.Ed.

Rickett.—On August 13, 1953, at Crowmarsh, Oxon., Gerald Russell Rickett, O.B.E., M.D.

Wood.—On August 6, 1953, in Sussex, John Alfred Wood, M.B., B.Ch., of 10, Canterbury Road, Oxford.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Ocular Signs of Drunkenness

Q.—*Is the reaction of the pupil helpful in establishing a diagnosis of drunkenness? In most cases I find the pupils widely dilated and only sluggishly, if at all, responsive to light. Is this due to a specific partial paralysis of the third cranial nerve? Could fright or fatigue account for this finding? Are there any other helpful ocular signs of drunkenness?*

A.—In this country it is generally accepted that the reaction of the pupil is helpful in establishing a diagnosis of drunkenness. In the early stages of alcoholic intoxication the pupils are dilated; they may be unequal. They often contract sluggishly and may dilate again in strong light even if the light is still directed into the eye. Swedish observers, however, state that the so-called slow reaction of the pupil is a normal phenomenon correlated with the original size of the pupil (Skoglund, C. R., *Acta physiol. scand.*, 1943, **6**, 96). In advanced intoxication and in coma the pupils may be pinpoint.

The changes in the pupil in alcoholic intoxication are probably due to the same mechanisms as the comparable changes seen during the stages of general anaesthesia. Since the early stage of alcoholic intoxication corresponds to the "excitement" stage of general anaesthesia, it seems likely that the dilated pupils are in part, at least, caused by an increased secretion of adrenaline. Depression of the parasympathetic system may also play a role. The dilatation of the pupil which occurs in fright is due to sympathetic overaction perpetuated by the secretion of adrenaline. Neither fright nor fatigue would usually give so prolonged an effect as occurs in alcoholic intoxication.

In drunkenness the eyelids are usually swollen and the conjunctivae suffused. Diplopia may occur, but strabismus can seldom be demonstrated by objective tests. Swedish observers regard the presence of nystagmus as the most valuable ocular sign of alcoholic intoxication. A fine lateral nystagmus is said to appear at blood alcohol concentrations of 0.08 to 0.10%. The sign disappears at concentrations of over 0.30%. Its absence is not therefore proof of the absence of alcoholic intoxication.

Recurrent Genital Herpes

Q.—*What is the best treatment of recurrent herpes genitalis? Would circumcision help? Is there any danger of a man who is about to marry infecting his wife?*

A.—The treatment of recurrent herpes is rather unsatisfactory, particularly the form occurring on the genitals. If the eruption is entirely limited to the prepuce circumcision would be worth trying, but not otherwise. Alternatively, the method of repeated smallpox vaccinations (eight times at fortnightly intervals) should be employed. There is, no doubt, a theoretical possibility of marital infection, but in actual practice this does not often seem to occur. The virus of herpes is very widespread throughout the human race, and it seems likely that recurrent attacks depend more upon the state of immunity of the subject than upon opportunities of infection with the virus. The disease, although a nuisance, is very seldom anything more; for this reason, the risk of marital infection need not be regarded with any great alarm.

Toxaemia of Pregnancy and Blood Groups

Q.—*Is there any known relationship between blood-group incompatibilities between husband and wife and the occurrence of toxaemia of pregnancy?*

A.—In the past it has been suspected that there might be a relationship between blood-group incompatibility between foetus and mother and the occurrence of toxaemia in the mother. However, it has never been established that there is such a relationship, and the general opinion is that incompatibility of this kind either plays no part at all, or, at the most, accounts for only a few cases.

Trichomonas Infection in the Male

Q.—*I suspect a husband of reinfecting his wife with Trichomonas vaginalis during intercourse. Is this likely in the absence of a urethral discharge? How should the diagnosis be made in the husband? What treatment should be given to the husband if my suspicions are correct?*

A.—Trichomonas infection may be present in the male without there being any obvious urethral discharge. The organisms can sometimes be demonstrated by scraping the epithelium just within the urethral meatus with a blunt curette, or in material obtained after prostatic massage. They have also been demonstrated in swabs taken from within the prepuce. In infected cases the urine is said to be typically hazy and containing fine threads; if it is centrifuged lightly the organisms can sometimes be found in the deposit. The material obtained by any of these means is preferably examined immediately both by means of a hanging drop preparation and by means of culture, for which a special medium is necessary. If there is any delay between collection and examination the swab should be kept moist with saline.

There is no specific remedy for trichomonas infection in the male. Various urinary antiseptics such as hexamine have been tried, and so have all the antibiotics and sulphonamides. None is of much value, although claims have been made for aureomycin. In fact there is a good deal of evidence to show that the infection is self-limiting in the male and that it disappears within three months and often in less time than this. The so-called chronic cases are probably examples of reinfection, husband and wife infecting each other in turn. This vicious circle can be broken by abstinence from coitus until the woman is cured, the infection in the male meanwhile dying out of its own accord.

Technique of Bronchography

Q.—*What is the best way of performing bronchography?*

A.—The selection of the method for bronchography depends on the situation and extent of the area required to be visualized. For example, the major bronchi in the right lower lobe can often be visualized by simply dropping the opaque medium over the back of the tongue while holding the tongue forward to prevent swallowing. This can be done without analgesia, but most people prefer analgesia of the nasopharynx and larynx. Lignocaine is the usual analgesic employed (in 4% solution as a surface analgesic for this purpose). A small piece of rubber tubing is passed through the nose until it rests just above the larynx. The tongue is held forward and the opaque medium slowly injected, tilting the patient to whichever side is necessary. This method is very successful for the right middle lobe and both lower lobes. It is not so successful for the upper lobes, except in the hands of an operator with wide experience.

Direct injection into the trachea just below the cricoid is probably the most effective method. Under local analgesia a fairly wide-bore needle is inserted into the trachea and a few drops of cocaine are injected through it to abolish the cough reflex before injecting the opaque medium. The needle is left *in situ* while the patient is tilted into the various positions.

Heavy viscous media are now being abandoned for bronchography because they remain in the lung for a very long period. Not only may they obscure subsequent alterations in a lesion, but they may also provoke an oil fibrosis. Water-soluble media are now available. These are quickly and completely absorbed, but they are temporarily rather irritating and deeper local analgesia is required to inject them successfully.

Death on the Table

Q.—*Who has the legal responsibility when a patient dies under an anaesthetic, the anaesthetist or the surgeon? Is there any difference between Scottish and English law in this connexion?*

A.—If a patient dies under anaesthesia, responsibility for the death does not necessarily rest upon either surgeon or anaesthetist. Legal responsibility, in the sense presumably intended by the question, will exist only if either surgeon or anaesthetist has failed in the proper execution of his functions as a skilled professional person.

An anaesthetist is an independent expert. Although not legally responsible if the death has resulted from a genuine and understandable error of judgment, he is expected to exercise a degree of skill, care, and judgment commensurate with his professional qualifications and experience. It is his responsibility to assess the fitness of the patient to support the strain of anaesthesia, to advise regarding premedication, to select a suitable form of anaesthesia, to ensure that the administration is satisfactory, and to have available and apply when necessary the appropriate measures for resuscitation. The decision to operate, the choice of operation, and the actual operative procedure is the responsibility of the surgeon, and, again, legal responsibility for a death will only exist if he has failed to exercise that degree of skill, care, and judgment which can reasonably be expected from a professional person of his particular qualifications and experience.

There is no difference between Scots and English Law in the matter. In both countries, the circumstances of the particular case would fall to be considered, and the important elements are, not understandable errors of judgment, but failure to exercise the requisite degree of judgment, skill, and care.

There is no case on record where criminal proceedings or a successful civil action has been taken against a medical man in respect of a death under anaesthesia, although there have been unsuccessful actions.

Diagnosis and Treatment of Congenital Syphilis

Q.—*What surveillance and treatment should be given to the baby of a syphilitic mother who (a) had no treatment during pregnancy; (b) was treated thoroughly during pregnancy?*

A.—(*a*) A baby born of a syphilitic mother who has had no treatment may or may not have contracted the disease, and it should be noted that in those that are born infected there may be no demonstrable *T. pallidum* or clinical manifestations. A child can also acquire the disease during parturition from a mother with an active lesion on the genitalia.

On the clinically normal infant serological tests should be carried out soon after birth and repeated one month, three months, six months, and 12 months later. If all these tests are negative it may be assumed that the child has escaped infection.

In the treatment of congenital syphilis the optimum dosage of penicillin has not yet been established. The dosage recommended varies from 100,000 to 300,000 units of procaine penicillin in arachis oil with 2% aluminium monostearate daily for 10–15 days. In the emaciated infant it is advantageous to give three-hourly injections of aqueous penicillin G (total dosage 200,000 to 600,000 units per kg. of body weight). It is not necessary to follow this up with arsenic or bismuth. Relapse, clinical or serological, is extremely rare, and in such cases the course of penicillin s repeated.

(*b*) Thorough treatment of a syphilitic mother during pregnancy will ensure a non-syphilitic baby, but serological tests should, as a precautionary measure, be carried out at the intervals stated above.

Efficiency of Inunction

Q.—*Some therapeutic substances are given by inunction. What is the evidence that they are absorbed through the skin and exert a pharmacological effect on the underlying tissues? I have in mind medicaments such as the creams which contain adrenaline, and the mercury inunction of former days. If it is true that certain drugs can penetrate the skin in this way, on what does this property depend?*

A.—The evidence that some therapeutic substances are absorbed through the skin is that they are excreted in the urine. Thus mercury can be detected in the urine within 24 hours of its inunction. Methylsalicylate can be detected in the urine within one hour. Sulphur and atropine are also absorbed through the skin when applied as ointments. Some say that iodine is, but some deny it. There is, however, no evidence that adrenaline is absorbed through the skin from a cream containing adrenaline. Drugs can readily be drawn through the skin into the general circulation by electrolysis, but as soon as they reach the dermis they are picked up by the blood stream and dispersed throughout the body. Absorption depends chiefly on physico-chemical properties rather than on chemical constitution. Substances to be absorbed must be soluble in both oil and water.

Masks for Industrial Dusts

Q.—*What are the best kinds of mask to use against industrial dusts, such as asbestos powder, which are irritating to the nose and throat? The patient in question develops a dermatitis when rubber is in contact with his skin.*

A.—The use of a mask for protracted periods to give protection against dust is not satisfactory, and protection against a dangerous dust such as asbestos should never be left to this means.

When temporary protection is required, however, the use of a dust respirator has value. The standard models are usually fitted with a rubber face-piece, but it is rare for the particular rubber used in these respirators to give rise to skin trouble. There is, however, on the market a much simpler respirator with an aluminium frame and employing cotton-wool as the filter. This is effective in stopping the inhalation of a certain amount of dust, but it has no official approval for use with asbestos. Many of these masks are to be seen at the Home Office Museum, in Horseferry Road, London, S.W.1, where it is also possible to see examples of effective methods of suppressing dust in industrial processes.

Correction.—In Dr. M. E. M. Herford's letter (*Journal*, August 22, p. 441) on breast-feeding in Oxford, the sentence, "Skin infections, particularly eczema, were not frequent in bottle-feds in each age group," should have read, "Skin infections . . . were more frequent in bottle-feds . . ."

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